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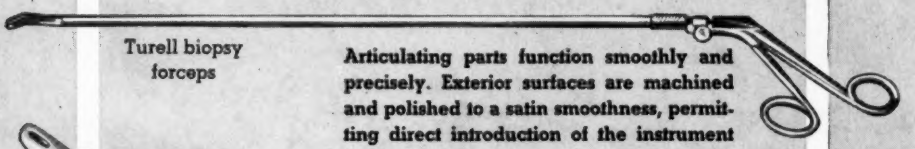

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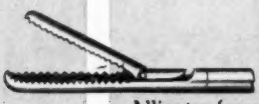

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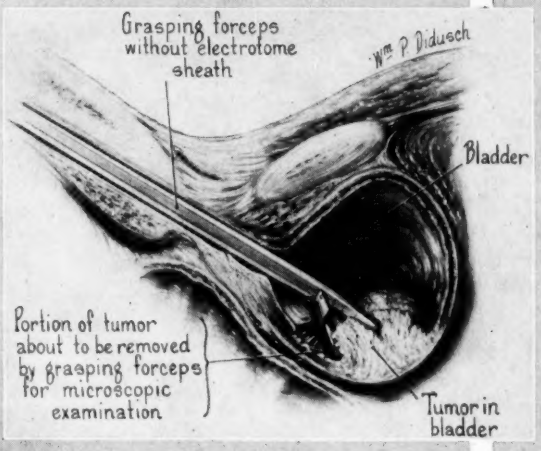
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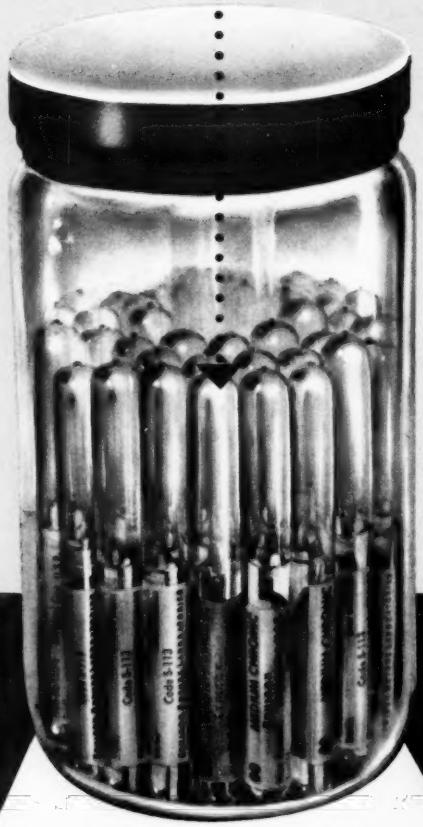

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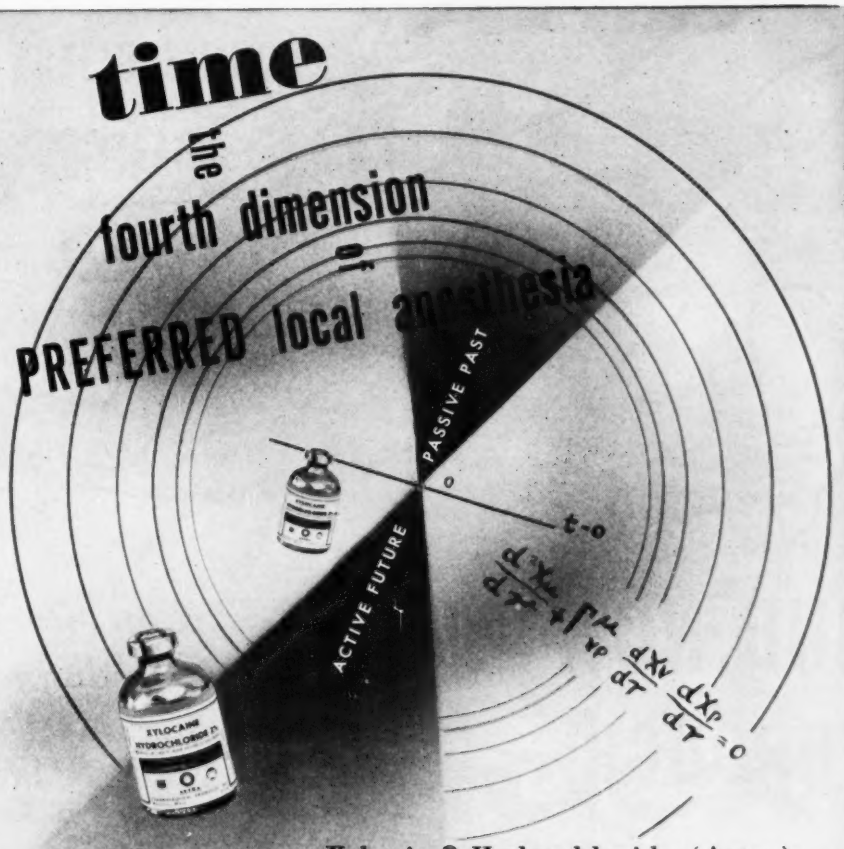

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VOLUME 66 MAY 1953 NUMBER 5

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Editorials

ARE GASTROJEJUNAL ULCERS DUE TO HYPERSECRETION?

GASTROJEJUNAL ulcers began to be observed shortly after the introduction of gastroenterostomy and have remained a serious complication of gastric surgery to the present time. Indeed, success in the treatment of duodenal ulcer is all too often cancelled by the development of a new ulcer in the jejunum adjacent to the anastomosis with the stomach, which may be more disabling and dangerous than the original disease. Recent observations in both the laboratory and the clinic have shed new light on the cause of gastrojejunal ulcer and form the basis for this editorial. The view that gastrojejunal ulcers, along with those occurring in the lower end of the esophagus, the stomach proper, the first portion of the duodenum, and in the ileum near the entrance of a Meckel's diverticulum containing heterotopic gastric mucosa, are peptic ulcers and are due to the corrosive action of the gastric content is widely accepted. The corrosive properties of the gastric content are almost entirely due to the pepsin and hydrochloric acid of the gastric juice and to a less extent to the mechanical and thermal effect of the food. Gastric juice is normally present in the stomach, and the absence of ulceration in normal people indicates that the mucous membrane can resist the corrosive properties of the usual gastric content, consisting of a mixture of food and digestive secretions. Theoretically, ulceration might occur either through a local decrease in the resistance of the mucous membrane of the stomach or duodenum or to an increase in the corrosive properties of the gastric content. Much work and speculation has so far failed to produce agreement as to whether spontaneous ulcers in the stomach or duodenum are due to one or the other or both these factors. In the case of gastrojejunal ulceration the problem appears to be more simple, if indeed the factors causing this complication are not already clearly in view. Ulcers in the first portion of the jejunum rarely occur spontaneously in an individual who has never been operated upon; on the contrary, they almost invariably are caused by a type of surgery which exposes the mucous membrane to the corrosive action of the gastric content. The problem of a specific or general decrease in resistance on the part of the mucosa therefore does not befog the problem in this case. When the secretion of gastric juice both in the empty stomach and in response to food-taking is within normal limits, the corrosive properties of the gastric content are not sufficient to break down the jejunal mucosa and produce ulceration. Thus stoma ulcer rarely or never occurs after gastrojejunostomy or gastroduodenostomy in normal dogs. It rarely or never follows gastrojejunostomy for the treatment of gastric ulcer or carcinoma of the lower part of the stomach. In these diseases the secretion of gastric juice is either

within normal limits or is depressed. The complication occurs almost solely as a result of gastroenterostomy or partial gastric resection, done for the treatment of duodenal ulcer. The data are now so extensive that it may be concluded that practically all patients with duodenal ulcer secrete more gastric juice, both in the fasting stomach and in response to the ingestion of food, than do normal people. Whereas, the mixture of gastric juice in normal amounts with food or with mucus, saliva, or duodenal content present in the stomach between meals produces a gastric content whose corrosive properties are not sufficient to break down the jejunal mucosa, the opposite is true when an abnormally large amount of gastric juice is present. Thus, gastrojejunal ulcers readily develop in dogs following gastroenterostomy, when a hypersecretion of gastric juice is induced by the implantation of pellets of histamine and beeswax into the subcutaneous tissues, as demonstrated by Wangensteen and his associates,[1] or when a hypersecretion of gastric juice of antrum origin is produced by the transplantation of the antrum into the colon as a diverticulum, as was reported from this laboratory.[2] The extremely rare occurrence of spontaneous peptic ulcer in dogs makes these observations of undoubted significance.

The experimental observations of Exalto,[3] that ulcers develop in dogs following a Roux-Y type of gastrojejunostomy, and of Mann and Williamson,[4] that ulcers develop after their method of internal duodenal drainage where the duodenal content is deviated into the lower ileum, are probably also in part due to this factor. The most widely accepted explanation for the cause of the Exalto and Mann-Williamson ulcers held that these were due to the deviation of the neutralizing alkaline secretions of the duodenum away from the region of the anastomosis. A difficulty in accepting this explanation as the sole cause of these lesions arose with the discovery by McCann[5] that ulcers still occurred even though the duodenal contents were deviated backward into the stomach rather than into the lower ileum. Under the conditions of McCann's experiment the alkaline duodenal contents were not deviated away from the region of the anastomosis. In some recent studies in our laboratory,[6] where the secretion of gastric juice by the stomach was determined quantitatively, the Mann-Williamson procedure was found to cause a profound hypersecretion of gastric juice of a degree comparable to that which in other experiments was found adequate to produce ulceration. Indeed, gastrojejunostomy itself[7] was found to stimulate gastric secretion if the anastomosis was made between the jejunum and the body or fundus of the stomach. No such hypersecretion resulted if the anastomosis was made between the jejunum and the stomach close to the pylorus, or in the gastric antrum. Disturbances in the physiology of the gastric antrum undoubtedly account for these effects, since they do not take place if the antrum has previously been excised. While the final physiological explanation must probably

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await further work, information at present available indicates that whenever gastric surgery for duodenal ulcer is performed these facts should be kept in mind. It seems apparent from our data that when vagotomy has reduced the secretion of gastric juice in the duodenal ulcer patient to normal limits gastroenterostomy is not followed by a higher incidence of gastrojejunal ulcer than occurs when the operation is done for patients with gastric ulcer or gastric carcinoma. Care, however, must be observed not to make the anastomosis too high on the stomach for fear that a hypersecretion of antrum origin might be induced. Procedures such as entero-entero anastomosis should be avoided in all types of gastric surgery for duodenal ulcer, since deviation of the alkaline duodenal contents away from the anastomosis is a potent, ulcer-forming procedure, operating probably both through hypersecretion and deficient neutralization. It may be concluded that the hypersecretion of gastric juice characteristic of the duodenal ulcer patient is the chief factor which causes gastrojejunal ulceration, and accordingly this complication may be expected when the definitive operation, whether it be vagotomy or gastric resection, has not been sufficiently complete to return the secretion of gastric juice to normal levels.

LESTER R. DRAGSTEDT, M.D.

REMAINING COMMON DUCT STONES AND THE RECURRENT BILIARY TRACT SYNDROME

CHOLECYSTECTOMY for chronic cholecystitis and cholelithiasis carries a mortality of 2% or less, in competent hands. Recently we reviewed a series of over 300 cholecystectomies in one of our hospitals without a surgical death where the disease and surgery were limited to the gall bladder. When choledochostomy becomes necessary, there is a step-up in the mortality rate. This is probably not due to the technical phase of the added procedure but to the complicated condition having affected other organs, particularly the liver and adjacent structures. We have never seen a stricture develop in a common duct from the mere incising of the common duct to place a T-tube, provided the T-tube was allowed to remain in place at least 10 days.

Stones escaping from the gall bladder and reaching the common duct markedly complicate the condition and affect the mortality rate. All gall-bladder stones are a hazard, but this does not necessarily mean that 100% of the patients with gallstones should have a cholecystectomy, although no doubt most of them should have the gall bladder and stones removed to avert their entering the group of patients with complications. In a few circumstances, cholecystectomy is not advised, but the possible complications and potentialities should be explained to the patient or the family.

Some stones reach the common duct in their original gall-bladder size. Others develop in the common duct from small particles of precipitate or debris which come from the diseased gall-bladder or disturbed bile physiology. Common duct stones very frequently elude the surgeon at the operating room table. Some 17 years ago we were making routine immediate cholangiograms at the table on all patients undergoing cholecystectomy. The presence of stones in the common duct in patients who had no symptoms of common duct disease and in whom a stone was not palpable was definitely proved. The development of the biliary flush, our

faith in it, and our end-results finally led to omitting the immediate cholangiographic studies. However, when a T-tube has been placed in the common duct, one should never omit taking a delayed cholangiogram. Every surgeon who has routinely made delayed cholangiograms on his patients has had the unhappy experience of finding remaining common duct stones and debris depicted on the films. The surgeon who does not take delayed cholangiograms following choledochostomy and believes it unnecessary remains in the dark as to how many stones he may have left during his career. It has been proved by autopsy studies that approximately 7% of patients with stones in the gall bladder have hepatolithiasis, and a certain percentage of these stones sooner or later reach the lower end of the common duct.

The recurrent biliary tract syndrome has practically disappeared in the group of cases in which the three-day biliary flush has been routinely used following cholecystectomy. This flush, created by the administration of hydrocholeretics and antispasmodics, is usually given about seven days following operation and is repeated two weeks later. When the delayed cholangiogram reveals stones or debris remaining in the common duct, the biliary flush regimen plus instillations or irrigations of substances through the T-tube has resulted in removal of any remaining debris in 70% of the patients. Warm saline, warm olive oil, ether, ether-alcohol mixture, chloroform, and other solutions have been used, and at present further evaluation of these solutions and research with other solutions is being carried out with encouraging information. After the removal of the T-tube, the flush is mandatory because the small particles which are found in the T-tube are also present in the common duct and these may be the nuclei for larger stones and obstructive symptoms.

R. Russell Best, M.D.

TRAUMA AND THE URINARY BLADDER

WITH AN ever-present influx of war injuries plus the increasing amount of civilian trauma, it becomes imperative that the surgeon who is called upon to treat trauma must consider the patient first as an injured *person,* not just a compound fracture of the tibia, a rupture of the spleen, or a fracture of the skull. Quite apart from the obvious local injury, other even more severe trauma may be present, a suspicion of which should be aroused in the mind of any well-trained surgeon. Furthermore, the patient as a whole reacts acutely to major trauma, not only with blood loss but also with biologic mechanisms set up by the alarm reaction and by what Moore has so ably described as an initial adrenergic corticoid period with an immediate disturbed metabolism.

Perhaps the organ most commonly missed is the urinary bladder. The "general" surgeon today is becoming more and more an intraperitoneal surgeon, but the urinary bladder is extraperitoneal. The orthopedist considers broken bones and, of course, does not presume to know anything about the urological department. The urologist is seldom called because the patient obviously has a fractured pelvis or an intra-abdominal injury. In an address before the American Association for Thoracic Surgery in May, 1952, I cited two instances of well-trained young surgeons who had completed formal surgical residencies at two of our better teaching hospitals but who did not know what to do when confronted by a patient with

a fractured pelvis, other than to call the orthopedic service. They showed an amazing forgetfulness of whatever they had been taught about the dangers of injury to the urinary bladder and simple methods of its diagnosis. This seemed so incredible that I have been asked if it were really true. Since then two other identical examples have come to my attention, and this convinces me more than ever of the need of reemphasizing such considerations.

1. I have been recently informed of a patient who was injured by an automobile and taken to an approved hospital in one of our large eastern cities. Inasmuch as he was a member of the Armed Forces, he was promptly put into an ambulance, with proper traction on a leg, and transferred to an Army hospital some 25 miles distant. No mention was made of possible bladder injury although the fractured pelvis had been recognized. An intraperitoneal rupture of the urinary bladder was found at operation in the latter hospital.

2. Recently, on our own service at Bellevue Hospital, a patient was transferred to us from another city hospital with a scalp laceration neatly sutured. In addition to this, the patient was in shock, and it was noted that he had a compound fracture of his tibia, which had been splinted. Since there was no room in the first hospital, he was transferred to us for further treatment. No attention had been paid to the crushing injury of his pelvis nor to the further fact that he had an extraperitoneal rupture of his bladder with obvious extravasation of urine. This was discovered only by examination at Bellevue Hospital and verified by operation.

3. As a third example, I might cite a patient whom I saw a number of years ago on the surgical service of a city hospital. While on a drinking bout, he had been injured in some manner unknown to himself. On coming to, he noticed a good deal of pain in his abdomen and reported to the hospital where a diagnosis of acute appendicitis was made and his appendix removed. A considerable amount of clear, free fluid was noted in the abdomen and only local injection of the serosa of the appendix. Some two months later, I was asked to see him in consultation because his appendix wound had not healed. As one approached the bed, a uriniferous odor permeated the air, and the dressings were soaked with a clear serous discharge coming from the McBurney incision. On questioning, the patient said that he had last voided prior to his drinking bout some two months previously! Fortunately, the Lord seemed to have a kindly regard for this particular individual and created a urinary fistula through the drainage tract that had been established by the surgeons.

Injuries to the urinary bladder have been recognized for a great many years, and in the horse and buggy days, "coachman's bladder" was a commonly accepted syndrome. This occurred in coachmen or truck drivers who were too comfortably ensconsced on their drivers' seats to get down to empty their bladders. In the course of going over a severe jounce or being thrown from their seats, as sometimes occurred, the hydrostatic pressure suddenly changed and the full bladder ruptured. The same thing occurs today, as in the case of a lady returning from the theatre one evening in a taxi and who thought she could wait until she reached the hotel. The taxi stopped suddenly, she was thrown to the floor and ruptured her bladder.

Rupture of the urinary bladder is not a serious injury if recognized promptly and treated properly. If neglected, however, the reverse is the case. In any injury

involving the pelvis or the spine, or a sudden crushing injury or fall which would result in a change of hydrostatic pressure, such a possibility must be recognized. The surgeon should always inquire if the patient had a full bladder at the time of injury. Accurate diagnosis may be made by relatively simple measures, such as blood in the urine, the passage of a catheter with negative results, and failure to obtain the return of simple sterile water or saline solution inserted into the bladder. Catheterization should always be performed in patients with back, abdominal, or pelvic injuries. A rupture of the bladder may be temporarily treated until further aid can be obtained by leaving the catheter *in situ* or establishing a simple suprapubic drainage. It is an injury all too often overlooked.

Any person who calls himself a surgeon should be competent in the initial surgery of trauma. This does not require the finesse of the specialties but does require a knowledge of normal anatomy, normal physiology, and the basic principles of sound surgery.

FRANK B. BERRY, M.D.

WHAT TO TELL THE PATIENT WITH PERSISTENT CANCER

THE CORRECT decision as to whether or not to tell the patient he has persistent cancer is frequently altered by the circumstances, personal, practical, and philosophical. In many instances, one decides that the patient is to be informed, and therein lies the reason for these words—solicited by an eminent surgeon from a most humble physician. To tell or not to tell—is that really the question? It appears to me that the manner in which the physician gives this information is of more importance than the information itself.

To be the bearer of bad tidings is a distasteful task at best, but to present the patient with an ill-defined prognosis and often, unfortunately, with certain limitations borders on the verge of cruelty. To those unfortunate ones who must face this task come varied thoughts on how to ease the burden to the patient and also to the physician. Let me tell you one such thought which has helped me considerably.

I prefer to have both husband and wife together at all such conversations, and early I introduce and then continue to maintain the combined husband-wife theme throughout.

After all, when one marries, the vows include ". . . in sickness and in health; for better or for worse. . . ." The presence of cancer in one member of a family is a problem for both and should be so stated. Almost invariably one or the other unaffected member of the family is acquainted with the important facts of the situation. To deny the husband or wife this information and to keep it "a secret" is to undermine the mutual confidence of the spouse which is the very foundation of a long and happy marriage. There are few real secrets between compatible man and wife; yet at the most crucial time in the life of the patient, when his very existence is endangered, the thin veil of secrecy is erected which threatens the future remaining happiness of the couple.

Perhaps this sounds impractical or trite, but I have employed it with almost universal success at every opportunity which has arisen.

A large number of intelligent patients become highly suspicious of the ominous persistence of symptoms and/or lesions. Some patients are better able to obscure this knowledge from the family and friends. Others are less capable of feigning their obvious concern; yet wishful, delusional thinking permits them to carry it off well. However, sooner or later, underneath it all, they will learn and confirm their worst suspicions, at which time they lose all confidence in those closest to them, who have betrayed their trust. The physician likewise is included.

If, on the other hand, the patient is introduced to the seriousness of his disease with the united front of the spouse and physician he realizes that he is not in the battle alone or unaided. His security is not threatened alone, but rather the threat is diluted by the reunion of confidences and further reassurance by those closest to him on the basis of forthright trust and understanding.

With single people or individuals who cannot share such a burden with a close relative, the physician can serve well in this capacity. He must encourage the trust and the understanding of the patient, not to the point of utter dependency but to a point of mutual confidence and encouragement.

When a patient is told he has cancer and that the prognosis is poor indeed, it is not necessary to pull all the props from underneath him. One must allow him a few straws of hope, and if there are none, it is up to the physician to create one. I have always been guided by the principle that I learned from a wise old surgeon: "Give the patient a straw upon which to cling; never take straws away from him." It matters little about the validity of "the straw." What matters more is the creation of hope and a look toward the future. It is the encouragement and desire to live on the foundation of this hope that permit the patient to go on and be a credit to his close friends as well as to himself.

We spend great sums of money and invest much time in care for the mentally ill who become dependent, and yet we heartlessly take a patient with a limited prognosis from a widespread cancer and brutally make him a recluse, causing him to draw within himself because in effect he has been shut off from the rest of the world. These are problems to be shared by all. The physician is the key to the situation, and fortunately it is a problem for the good doctor—the surgeon and internist alike.

HOWARD R. BIERMAN, M.D.

PSYCHOPHYSIOLOGY OF THE DUMPING SYNDROME

THE NUMBER of patients requiring a subtotal gastric resection for gastric and duodenal ulcers or neoplasms of the stomach is increasing. This enlarges the number of individuals who may be bothered with the so-called dumping syndrome. We do not yet know all the answers to this problem. This is obvious from the number of papers being published all the time describing new technical procedures in an effort to overcome this syndrome. It seems to me, however, that the surgeon, if he will take a little time, can do a great deal to relieve his patients of these symptoms.

At the University of California Medical Center, an increasing number of patients are coming to us who have had gastric resections done elsewhere. Most of them have been definitely improved, but it is amazing to see how many are still bothered

considerably by the dumping syndrome. Much of this distress could have been avoided had the surgeon simply taken enough time to sit down and talk to his patients about their condition, making a little rough sketch as to what the normal stomach and duodenum look like, describing what was done in order to cure their original difficulty, and explaining why they are having these symptoms following their operation. When the point is stressed that nearly always this discomfort eventually disappears, it is astonishing to hear and see the number of patients who say, "Oh well, if it is not going to last indefinitely then I can put up with it. Why didn't Dr. So-and-so explain this to me?"

I have found too that these patients are often given a long list of foods and sent home on a certain type of diet. It has been my experience that many of them come back in a month or two and ask, "Doctor, may I have such and such food?" When questioned, they usually say they have already tried it and that the food has not bothered them. As a rule, my advice to such patients is that it is perfectly all right for them to have the food they have asked about since no two individuals are alike, and a patient's craving for a particular food in all probability means that it will agree very well with him. Many times a patient can be his own dietician better than we can.

These comments do not mean that all of my own patients are free of the dumping syndrome. However, so far I have been able to carry them along to the point that these symptoms are of no real trouble or concern to them.

My only reason for putting these remarks down on paper is that it seems to me too much of a tendency exists nowadays for well-trained and qualified Board surgeons to feel that once they have done a good technical surgical procedure, they no longer have any responsibility to their patients. In other words, I think a surgeon has to be a doctor first and a surgeon second. Otherwise, he is not a complete unit. I do not mind doing the explanations for other surgeons, but it seems to me that the individual who operates upon a patient should be closer to that patient than anyone else. It is up to him, I believe, even though he may be a very busy surgeon, to take the time to answer the questions that come up in the patient's mind and not try to slough them off on someone else who does not talk the same language as the surgeon.

These patients are not psychoneurotics. They should not be sent to a psychiatrist. The surgeon should do his own practical common-sense psychiatry by listening and talking to his patients.

H. GLENN BELL, M.D.

FIBROBLASTIC STIMULATION OF RABBIT ARTERY ADVENTITIA BY MARINE VARNISH, "KRYLON," and LATEX

Laboratory Study Related to the Surgery of Congenital Cerebral Aneurysm

BARNES WOODHALL, M.D.
AND
JAMES GOLDEN, M.D.
DURHAM, N. C.

AFTER the observation in man that leakage from a small aneurysm induced thrombosis within and around the sac, Dott first attempted operative reinforcement of what he termed, "Nature's attempt at healing."[1] On April 22, 1931, Dott exposed a congenital cerebral aneurysm at the junction of the anterior and middle cerebral arteries, which promptly ruptured. The hemorrhage was controlled by a pledget of leg muscle, and the arteries and the aneurysm were subsequently surrounded by thin sheets of muscle. This case was reported two years after operation, and at that time the patient was well. In our series of 57 congenital cerebral aneurysms treated by an intracranial operative procedure, 4 have been packed by muscle or with oxidized cellulose, as described by Dott. In two of these cases a recurrent subarachnoid hemorrhage occurred.

As a result of this experience in the human being, a number of tissue irritants have been considered as feasible agents for the strengthening of arterial wall either through periadventitial fibrosis or through their actual alloplastic action. Those tissue irritants reported in this preliminary note include marine spar varnish, composed essentially of a bakelite® gum and pure China tung oil, "krylon," a liquid plastic, and natural Hevea latex, with a total solid content of 65.5% and preserved in NH_3 to a percentage of 0.7.

EXPERIMENTAL METHOD

With use of intravenous injections of pentobarbital (nembutal®) anesthesia, the ventral surfaces of the lower extremities of adult gray rabbits were shaved and surgically cleansed. A short incision exposed the ventral neurovascular bundle of the thigh, including the great saphenous artery, the great saphenous vein, and the greater saphenous nerve, lying between the bellies of the adductor magnus and the

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Public Health Service Research Fellow of the National Heart Institute (Dr. Golden).

Presented at the Surgical Forum, Clinical Congress, American College of Surgeons, New York, 1952.

1. Dott, N. M.: Intracranial Aneurysm: Cerebral Arterioradiography; Surgical Treatment, Tr. Med.-Chir. Soc. Edinburgh **40**:219-240, 1933.

vastus medialis muscles. The artery was stripped of adjacent tissue and 5 drops of the test substance placed upon and about the neurovascular bundle. The operative field was exposed to room air for approximately two to three minutes without specific attention being directed toward drying. The muscle was closed over the test area with two fine nonabsorbable surgical (silk) sutures and the skin wound closed. The opposite thigh was used as a second test experiment or as a control. The animals were killed at 7, 14, and 21 days by means of pentobarbital given intravenously. The operative areas were removed in a single block, fixed in Zenker's fluid, and imbedded in paraffin. Sections were prepared with hematoxylin and phloxine, Masson trichrome, and Van Gieson stains. Fifty-one experimental preparations and appropriate controls were studied.

Gross Findings.—Marine Varnish: The varnish appeared to adhere to the vessel wall but did not dry during the short period of application. The gross specimens showed white caseous material at the site of application, extending into adjacent fascial planes. The distal arterial segment bled freely in all of 19 preparations.

"Krylon": With "krylon," as with marine varnish, the distribution of the material could not be visualized easily at the time of application. Adherence to the vessel wall was adequate, but no drying occurred during the time of application. There was no evidence of arterial thrombosis in 16 preparations. The gross specimens showed some fragmentation of the plastic. There was a marked inflammatory reaction at the site of implantation, similar to that noted with marine varnish.

Latex: Latex, because of its distinctive white color, could be applied to the vessel wall, under visual control. Adherence to the vessel was good, but drying did not occur during the time of application. There was a marked inflammatory response, and small elastic fragments of latex could be seen at the time of block removal. The distal arterial segment was patent in all of 16 preparations.

Microscopic Findings.—Marine Varnish: The immediate inflammatory reaction was particularly marked in adjacent muscle but was not striking about the neurovascular bundle. Scattered foreign body cells were present. At 21 days, there was in the majority of preparations rapid clearing of the inflammatory reaction, with the production of minimal periarterial fibrosis (Fig. 1).

"Krylon": Sections at all three time periods showed considerable foreign body reaction, with an early inflammatory process. Circular and linear spaces about the vessel suggested solution of the plastic during preparation of the sections. The inflammatory reaction subsided rapidly, with a moderate degree of residual fibrosis (Fig. 2).

Latex: The early inflammatory reaction was evenly distributed about the arterial wall and appeared to invade the adventitia. The cell type was mononuclear, showing considerable phagocytosis followed by the deposition of collagen. The 21-day preparations showed a uniform and thick fibrosis of adventitia and surrounding tissues (Fig. 3).

In these, as with the other tissue irritants, endothelial proliferation was variable from animal to animal and in terms of time. From the study of controls, it apparently represents a species variable. No alterations in structure were noted in the adjacent peripheral nerve tissues.

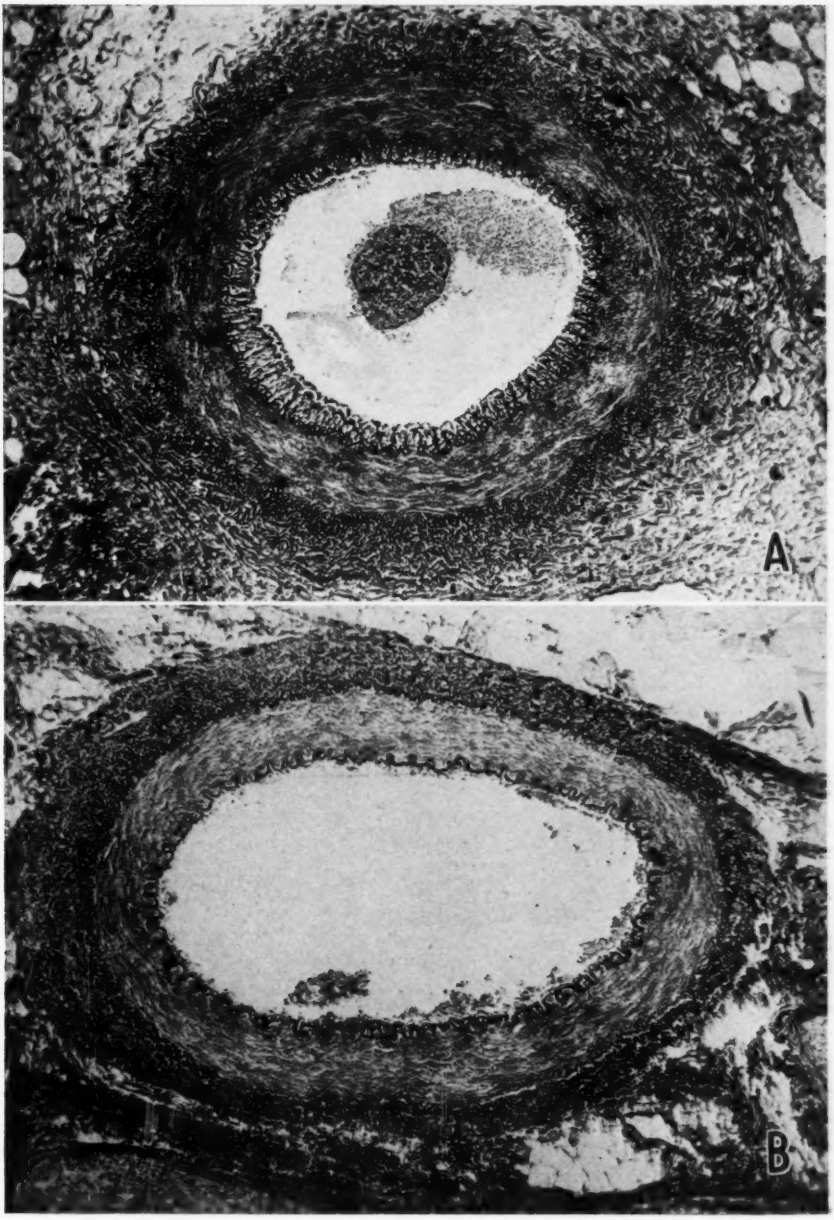

Fig. 1.—*A*, moderate inflammatory reaction about arterial wall at seven days; marine varnish. *B*, resolution of inflammatory response to marine varnish at 14 days, with minimal fibrosis about adventitia.

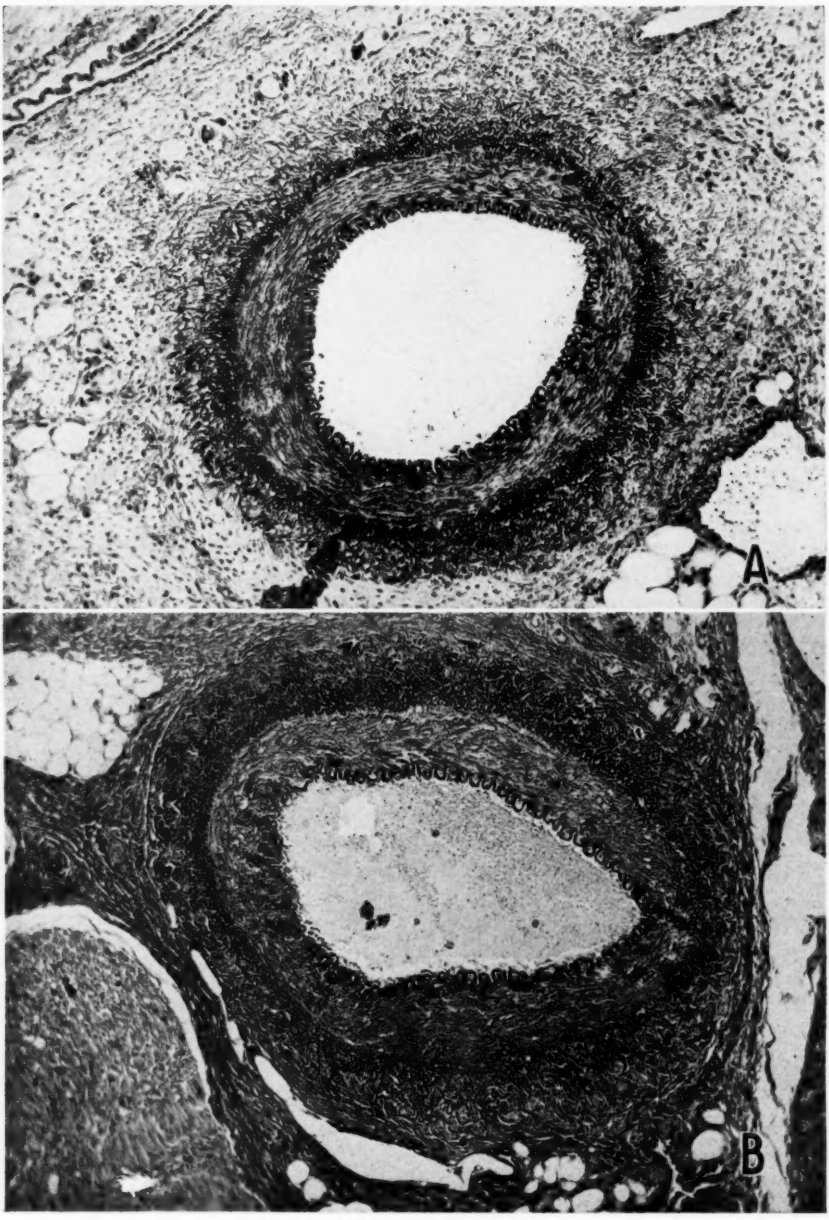

Fig. 2.—*A*, moderate inflammatory reaction and foreign body reaction about vessel wall with "krylon" at seven days. *B*, irregular, but moderately extensive, fibrosis about adventitia of arterial wall with "krylon" at 21 days.

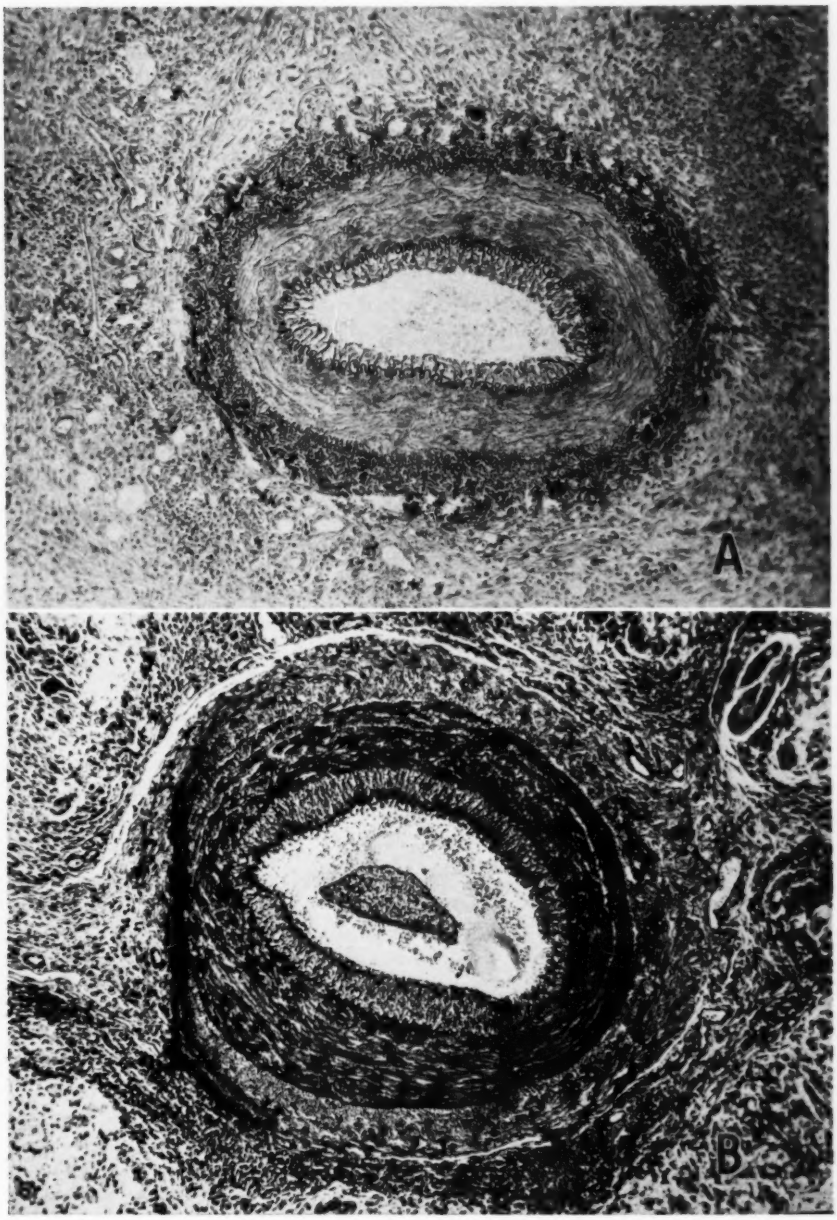

Fig. 3.—*A*, evenly distributed, adherent, and moderately intense inflammatory reaction about adventitia of vessel wall with latex at seven days. *B*, firm dense fibrosis about adventitia of vessel wall with latex at 21 days.

COMMENT

Intravascular pressure studies of inadequate cross circulation in the circle of Willis have demonstrated in an objective way that certain congenital cerebral aneurysms cannot be treated by complete ligation of the involved vessel either by an extracranial or intracranial ligation.[2] Such aneurysms can be controlled only ineffectively by partial carotid ligation or by the muscle-packing technique advocated by Dott.

These preliminary investigations in the rabbit suggest that natural Hevea latex may be a substance that can promote thickening of arterial walls without intrinsic alteration of that vessel's function. The adhering power of latex to damp arterial wall may be enhanced by previous weak acidification of the vessel wall, a variation in application that may add tensile strength to the treated vessel. This study and the reaction of the brain to latex will be reported in future papers.

2. Woodhall, B.; Odom, G. L.; Bloor, B. M., and Golden, J.: Direct Measurement of Intravascular Pressure in Components of the Circle of Willis: A Contribution to the Surgery of Congenital Cerebral Aneurysms and Vascular Anomalies of the Brain, Ann. Surg. **135**:911-922, 1952; Studies on Cerebral Intravascular Pressure, J. Neurosurg. **10**:28-34, 1953.

PREVENTION OF EXPERIMENTAL ESOPHAGEAL STRICTURE BY CORTISONE

II. Control of Suppurative Complications by Penicillin

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NEW BRUNSWICK, N. J.

IN A PREVIOUS communication,[1] it was shown that when large doses of cortisone were administered to rabbits after chemical (sodium hydroxide) burns of the esophagus, the tendency to fibrous stricture formation was remarkably diminished. This antifibroplastic action of cortisone was accompanied with high morbidity and mortality resulting from serious suppurative infection, mostly intrathoracic, i. e., pneumonia, empyema, lung abscesses, etc. Such infections were rare or nonexistent in the control group. The amounts of cortisone employed were equivalent to 420 to 560 mg. per day for a 70 kg. human being, and the poor survival rate seemed related to the large amount of hormone employed.

The increased tendency to infection associated with the administration of cortisone in large amounts has been well documented in the literature. Thus, in 1950, Antopol [2] reported a high incidence of "spontaneous" infections in mice treated with massive doses, while his control mice showed no such incidence even when placed in the same cage with the cortisone-treated group. He concluded that cortisone may have exhausted protective mechanisms, with depletion of immune bodies. In the clinical use of cortisone and corticotropin, intercurrent infections have been observed frequently, including gluteal abscess, furunculosis, acute bronochopneumonia, pneumococcal peritonitis, pulmonary mycosis, empyema, and Staphylococcus sepsis.[3] Armstrong and Irons [4] reported instances of clinically unsuspected cortical abscesses of the kidney and suppurative pericarditis in patients receiving cortisone

Aided by a grant from Merck & Company, Rahway, N. J.

From the laboratories of the St. Peters General Hospital.

1. Rosenberg, N.; Kunderman, P. J.; Vroman, L., and Moolten, S. E.: A. M. A. Arch. Surg. **63**:147, 1951.

2. Antopol, W.: Proc. Soc. Exper. Biol. & Med. **73**:262, 1950.

3. Hench, P. S.; Kendall, E. C.; Slocumb, C. H., and Polley, H. T.: Arch. Int. Med. **85**:545, 1950. Beck, J. C.; Browne, J. S. L.; Johnson, L. G.; Kennedy, B. J., and MacKenzie, D. W.: Canad. M. A. J. **62**:423, 1950. Soffer, L. J.; Levitt, M. F., and Baehr, G.: Arch. Int. Med. **86**:558, 1950. Carey, R A.; Harvey, A. M., and Howard, J. E.: Bull. Johns Hopkins Hosp. **87**:425, 1950.

4. Armstrong, S. H., Jr., and Irons, E. N.: A. M. A. Arch. Ophth. **45**:251, 1951.

or corticotropin. Kirsner and Palmer [5] report a case in which peritonitis was recognized after corticotropin therapy had been begun and in which the patient died despite the administration of large doses of antibiotics.

In view of the possible clinical application of cortisone in the therapy of accidental lye burns of the human esophagus, it seemed desirable to evaluate the protective influence of antibiotics in rabbits to which cortisone was administered after experimental alkali burns of the esophagus. Penicillin was selected for use in the present series.

TECHNIQUE

The technique employed was essentially that described in our previous communication and is briefly summarized below.

Rabbits of medium size (about 2.5 kg.) were anesthetized with open drop ether, and an olive-tipped metal bougie was gently guided into the esophagus. An infant-sized esophagoscope was threaded over the bougie, and the latter was then withdrawn. Under direct vision the posi-

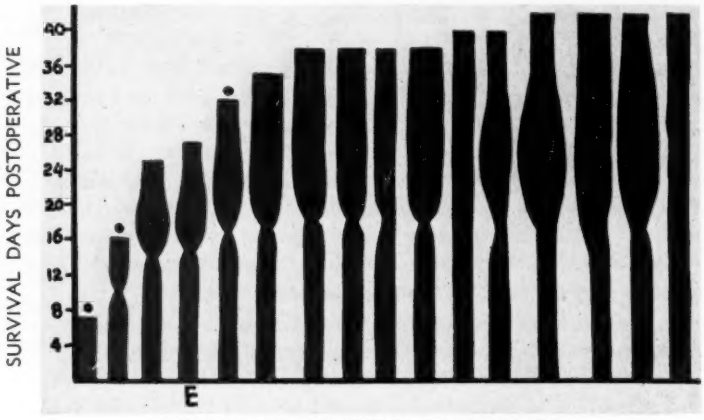

Fig. 1 (No treatment).—Each esophagus in this and in succeeding figures is shown semidiagrammatically, the survival time to death or time the animal was killed being represented by the height of the specimen illustrated. ●, died; *E*, empyema. Note high incidence of stricture, good survival rate, and low incidence of suppurative infection.

tion of the instrument within the esophagus was checked and a cotton-tipped applicator, saturated with 5% sodium hydroxide solution, was introduced to a point just beyond the distal end of the esophagus. Gentle circular swabbing of the esophageal mucosa was then carried out for 60 seconds, after which the applicator and the esophagoscope were withdrawn.

The animals were divided into the following three groups.

Group I, controls (16 animals). These rabbits received no treatment after the production of esophageal injury.

Group II, cortisone only (23 animals). These rabbits received cortisone (cortone® [6]) subcutaneously in doses of 6 to 8 mg. per kilogram of initial body weight, with gradual reduction in the dose after the first two weeks and discontinuation of the medication after the fourth week. In most instances the first dose was given about one hour after the alkali injury.

Group III, cortisone-penicillin (21 animals). Rabbits in this group were treated as outlined for Group II and were given, in addition to cortisone, procaine-penicillin in oil by injection,

5. Kirsner, J. B., and Palmer, W. L.: J. A. M. A. **147**:541, 1951.

6. Supplied by Dr. Augustus Gibson, Executive Director, Medical Department, Merck & Company, Inc., Rahway, N. J.

100,000 units every other day intramuscularly for two weeks. All animals were offered their usual diet of food pellets and water, no other special care being given them. Those animals which were killed in good condition were considered as "survivors."

RESULTS

Group I.—Controls: Esophageal stenosis occurred in 12 of 15 animals surviving long enough (two weeks or longer). One rabbit died on the seventh day and showed no stricture; one was killed in the sixth week and showed only slight narrowing, and two showed no narrowing whatever after six weeks (Fig. 1). The high incidence of stricture is noteworthy in the face of the high proportion of long-term (six-week) survivors and the low incidence of intercurrent infection.

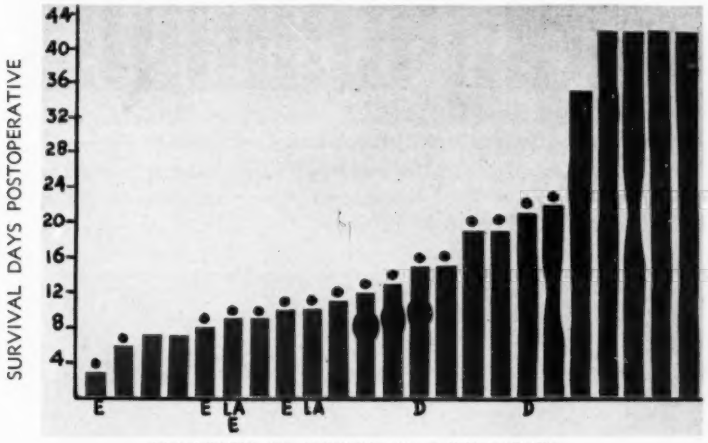

Fig. 2 (Cortisone only).—●, died; (●), perforation and mediastinitis; *LA*, lung abscess; *D*, diarrhea; *E*, empyema. Note low incidence of stricture, poor survival rate, and high incidence of suppurative infection.

Therapy

Days After Injury	CONTROLS Cortisone*	CORTISONE ONLY Cortisone* Mg./Kg. (Subcutaneously)	CORTISONE AND PENICILLIN Cortisone* Mg./Kg. (Subcutaneously)	CORTISONE AND PENICILLIN Procaine-Penicillin, Units (Intramuscularly)
1- 2	None	8, daily	8, daily	100,000, every 2d Day
3-14	None	6, daily†	6, daily	100,000, every 2d Day
15-21	None	4, daily	4, daily	None
22-28	None	4, alternate days	4, alternate days	None

* Cortone.®
† Equivalent to 420 mg. for a human being weighing 70 kg. (154 lb.).

Group II.—Cortisone Only: Of 23 animals in this group (Fig. 2), only 2 of 11 surviving two weeks or longer showed slight narrowing of the esophagus. However, 16 animals of this group died during the course of the investigation, and autopsy revealed a high incidence of intercurrent suppurative disease, chiefly intrathoracic. Empyema occurred three times; lung abscesses with fibrinous pleuritis, once; liver abscess, once, and death following severe diarrhea, twice.

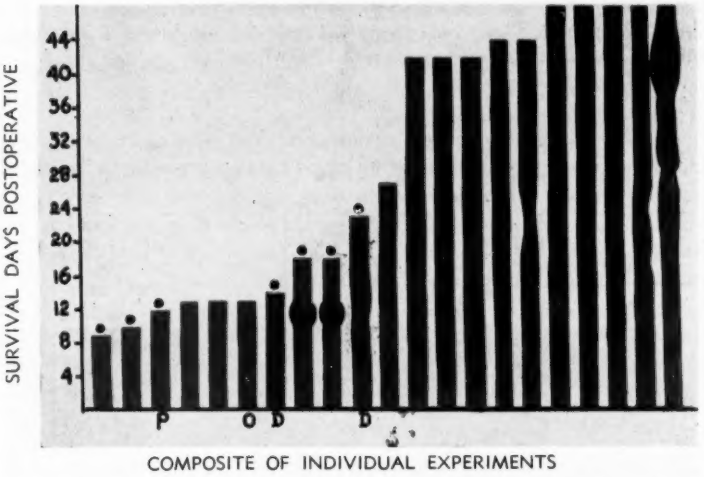

Fig. 3 (Cortisone and Penicillin).—•, died; (•), perforation and mediastinitis; *P*, pneumonia; *O*, ear infection; *D*, diarrhea. Note low incidence of stricture, improved survival rate, and lowered incidence of suppurative infection.

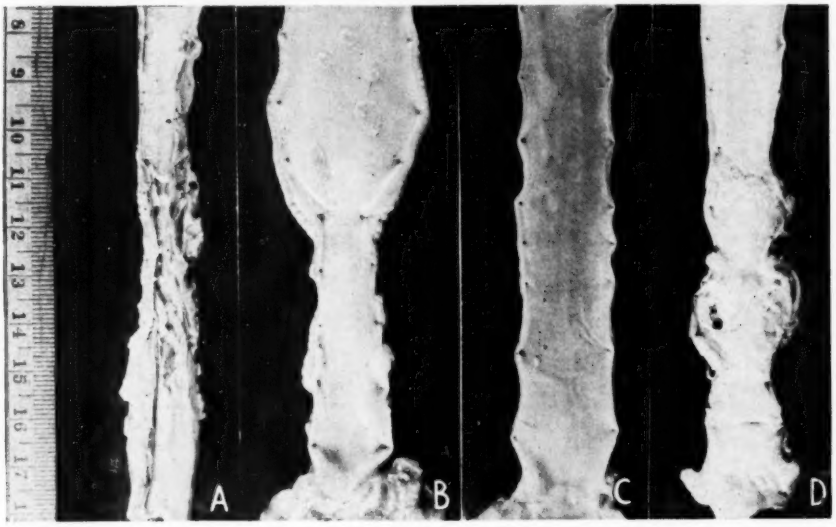

Fig. 4.—Specimens photographed after fixation in formaldehyde. *A*, control esophagus 36 hours after sodium hydroxide burn. Note extent of lesion, edema, and superficial necrosis with ulceration. *B*, control esophagus at 27 days. Note sharply localized stricture with thickening of submucosal tissues and marked proximal dilation. *C*, cortisone-treated esophagus, 44 days after injury. Note absence of stricture and almost normal caliber of esophagus. *D*, cortisone-treated esophagus. Ulceration with perforation of esophagus, mediastinitis, and empyema. Rabbit died 13 days after chemical injury.

In three instances spontaneous perforation of the esophagus took place through the ulcerated burn area, with death from mediastinitis in the second or third week after injury.

Group III.—Cortisone-Penicillin: In this series of 21 rabbits, only one instance of esophageal stricture and two instances of slight esophageal narrowing were observed (Fig. 3). At the same time striking improvement in mortality figures with an approximately twofold increase in the number of long-term survivors was observed.

Only four animals of this group presented evidence of infection. Three of these died, two with diarrhea and one with pneumonia. Nonfatal external otitis was seen in one rabbit. The two instances of fatal diarrhea might conceivably have been caused by penicillin-insensitive enteric organisms. In addition, spontaneous esophageal perforation with fatal mediastinitis was seen in two rabbits, as in Group II.

COMMENT

The results obtained in our previous paper [1] have been further amplified in this larger series of experiments. Cortisone, administered in large doses shortly after injury, has been shown to diminish markedly the tendency to stricture formation following alkali burn of the rabbit esophagus. Antifibroplastic effects have been obtained experimentally by others.[7] A recent paper reporting the effectiveness of somewhat smaller amounts of cortisone in preventing ureteral stricture also deserves mention here.[8]

The increased incidence of serious intercurrent infection, mostly suppurative in nature, and the associated high mortality in the group of animals receiving cortisone without penicillin further corroborate the findings of other investigators.

What seemed most striking was the effectiveness of penicillin, a "narrow spectrum" antibiotic (chosen because of its ease of administration), in reducing both the incidence and the mortality of infections in animals receiving cortisone.

The occasional occurrence of spontaneous perforation through the area of sloughing esophageal ulceration in the second or third weeks, usually with death from suppurative mediastinitis, even in animals receiving penicillin, seems to be a problem of somewhat different nature. The following factors may have contributed to the development of such perforations: 1. The animals were given a normal diet of hard food pellets after the burn. 2. Regurgitation of gastric juice may have superimposed acid peptic digestion upon the immediate destructive action of the sodium hydroxide. 3. The antianabolic antifibroplastic effects of cortisone presumably retarded the laying down of a granulation tissue barrier which might have prevented perforation. 4. In a number of cortisone-treated rabbits the esophagus presented an almost translucent appearance, when compared with controls, increasing still further the natural delicacy and thinness of the esophageal wall of these small animals.

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7. Ragan, C.; Howes, E. L.; Plotz, C. M.; Meyer, K., and Blunt, J. W.: Proc. Soc. Exper. Biol. & Med. **72**:718, 1949. Howes, E. L.; Plotz, C. M.; Blunt, J. W., and Ragan, C.: Surgery **28**:177, 1950. Spain, D. M.; Molomut, N., and Haber, A.: Am. J. Path. **26**:710, 1950. Baker, B. L., and Whitaker, W. L.: Endocrinology **46**:544, 1950. Stinchfield, F. E.: J. Bone & Joint Surg. **32**-a:739, 1950.

8. Baker, R.; Govan, D., and Huffer, J.: Surg., Gynec. & Obst. **95**:446, 1952.

The reported exacerbation and perforation of existing peptic ulcers of the stomach and duodenum during treatment with cortisone or corticotropin in man [9] are clearly paralleled in these experiments in the rabbit esophagus, wherein it has been shown that ulceration may similarly progress to perforation during therapy with large doses of cortisone.

It would seem from these observations that further study is required before the potent antifibroplastic action of cortisone can be safely directed to the therapy of acute lye burns of the human esophagus. Certainly it would seem that broad-spectrum antibiotics in large doses would be a necessary adjuvant, also bland liquid feedings, including antacids, methantheline (banthine®) bromide, or similar agents. Daily roentgen studies of the mediastinum, with or without contrast material, would be mandatory during the first two weeks after the burn to permit early detection and appropriate drainage of the mediastinum in the event of perforation.

The usual poor preservation of esophageal function after accidental lye ingestion in man, may, however, make further investigation of the unique properties of cortisone important.

SUMMARY AND CONCLUSIONS

Cortisone is a potent inhibitor of the tendency to scar-tissue contracture in the rabbit esophagus following experimental sodium hydroxide burn. Large doses of the hormone were employed to produce this effect.

The use of such large doses of cortisone is associated with high morbidity and high mortality due to intercurrent suppurative infections, mostly intrathoracic.

The administration of penicillin concurrently with cortisone has been shown to diminish markedly the incidence of infection and to influence favorably the mortality figures.

Spontaneous perforation of the ulcerated esophagus occurred in 5 of 44 rabbits under cortisone administration. Possible mechanisms underlying these perforations are discussed.

The application of cortisone therapy in acute lye burns of the human esophagus is discussed in the light of these hazards.

ADDENDUM

In a recent paper by Weisskopf [10] the successful employment of cortisone in the treatment of an acute lye burn of the human esophagus is documented. The patient, a 17-month-old boy, received 25 mg. of cortisone (cortone®) and 500 mg. of terramycin every six hours for three days, followed by continued administration of cortisone at 12-hour intervals until the 12th day, when the supply of hormone was exhausted.

Shallow ulcerations were seen on esophagoscopy during the acute phase after injury, but no stricture developed, and no dilation has been required. Weisskopf stated that antibiotics were important adjuvants in the clinical management of this patient. He also studied experimental sodium hydroxide burns, with and without cortisone therapy, in 15 dogs, with results similar to those described in our present and previous papers, except that esophageal perforation was not observed. Suppurative complications were not prominent in his animals, all of which, however, received terramycin.

9. Habif, D. V.; Hare, C. C., and Glaser, G. H.: J. A. M. A. **144**:996, 1950. Smyth, G. A.: J. A. M. A. **145**:474, 1951.

10. Weisskopf, A.: Ann. Otol. Rhin. & Laryng. **61**:681, 1952.

ANATOMY OF THE BILIARY DUCTS WITHIN THE HUMAN LIVER

Analysis of the Prevailing Pattern of Branchings and the Major Variations of the Biliary Ducts

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AND
PAUL C. SCHROY, M.S.
PHILADELPHIA

THE ANATOMY of the biliary system has been the subject of extended research for many years. Largely because of their surgical importance in cholecystectomies and the ease with which they may be studied, interest has been centered on the extrahepatic bile ducts, while comparatively little attention has been given to the gross morphology of the bile ducts within the liver.

Prior to 1888, anatomists, other than histologists, directed their attention chiefly to the external morphology of the liver. In that year, Hugo Rex [1] made the first attempt to study the intrahepatic course of the vascular and biliary channels by the injection-corrosion method. He investigated the livers of various mammals, including man, but he did not cite the number of human specimens observed, the number probably being very few as judged from the text. It was not until 1924 that a publication appeared which was concerned specifically with the intrahepatic anatomy of the adult human liver, namely, the work of Melnikoff.[2] Although both Rex and Melnikoff gave very extensive descriptions of the vascular systems, they dealt but briefly on the course and branchings of the bile ducts. McIndoe and Counsellor [3] in 1927 made a study of the intrahepatic ducts in 42 human livers. While they failed to describe the mode of branching of the intrahepatic ducts, they did reemphasize the concept of the bilaterality of the liver, as first suggested by Cantlie [4] in 1898.

Interest in the intrahepatic anatomy was revived in recent years by Hjortsjö,[5] who, in 1948, made studies of the ductal system by means of corrosion specimens

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2. Melnikoff, A.: Architektur der intrahepatischen Gefässe und der Gallenwege des Menschen, Ztschr. Anat. **70**:411, 1924.

3. McIndoe, A., and Counsellor, V.: Bilaterality of the Liver, Arch. Surg. **15**:589, 1927.

4. Cantlie, J.: On a New Arrangement of the Right and Left Lobes of the Liver, Proc. Anat. Soc. Great Britain & Ireland **32**:4, 1898.

5. (*a*) Hjortsjö, C.: Die Anatomie intrahepatischen Gallengänge beim Menschen, mittels Röntgen- und Injektionstechnik studiert, nebst Beiträgen zur Kenntnis der inneren Lebertopographie, K. fysiogr. Sällsk. handl. **59**:1, 1948; (*b*) The Topography of the Intrahepatic Duct System, Acta anat. **11**:599, 1951.

and cholangiograms. The limited number of specimens investigated and the cumbersome and confusing Latinized terms employed make the interpretation of this work extremely tedious and difficult. Hjortsjö, however, did originate the concept that the branching of the biliary ducts follows a segmental pattern, in the sense that each region of the liver has its specific type of bile drainage. To obtain a better interpretation of cholangiograms with relation to hepatic disease, Fainsinger,[7] in 1950, investigated the normal pattern of the hepatic ducts in 35 human livers by the injection-corrosion method and roentgenograms. His observations and conclusions will be considered in our discussion. More recently, Elias and Petty [8] studied the intrahepatic anatomy in 18 livers. Like other investigators, they emphasized the vascular structures but failed to give a description of the bile ducts.

We began this work before realizing that Hjortsjö had emphasized the concept of segmentation of the liver. Upon observing an injected specimen of the biliary system, we noted the very striking pattern suggestive of a segmental branching and so proceeded with this study.

MATERIAL AND METHOD

The hepatic ducts were studied in 100 adult human livers which were obtained at autopsy from the departments of pathology, of the Jefferson Medical College Hospital and the Pennsylvania Hospital. The common hepatic duct was dissected in each specimen in the region of the porta hepatis. The ductal system was perfused with water under pressure and then dried by the injection of acetone and air. A 15% solution of vinyl acetate, containing 10% (by weight) barium sulfate, was injected into the ducts under fluoroscopic vision. This afforded us an opportunity to study these ducts as they were filling and also assured us that all parts of the liver had been reached.

After the injection of the hepatic duct system, a roentgenogram was taken. The plastic was then allowed to harden overnight, and on the following morning a reinjection of the ducts was carried out. On the third day, the liver was placed in a concentrated solution of hydrochloric acid for from one to three days. After removal from the acid, the specimen was washed with water to remove the remaining hepatic parenchyma, and the casts were then ready for study.

In three of the livers of this series it was impossible to inject fully the right hepatic duct system because of damage to the right main duct during removal of the organ at autopsy.

OBSERVATIONS

In describing the hepatic duct passageways it is necessary to name the main branches. We have chosen to use a directional nomenclature, and in doing so we will try to conform with the suggestions which the Nomenclature Committee of the Thoracic Society made with regard to an international bronchopulmonary directional nomenclature.[9] The committee advised using terms which would be understood by all and not only by specialists. The terms should conform with anatomic arrangements which have been established and with the usual terms used in descriptive anatomy. They should be as simple as possible and of such a nature as to be easily translated into other languages. It is with these suggestions in mind that we have used our directional terms in the description of the hepatic ducts.

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6. Footnote delected.

7. Fainsinger, M.: The Radiology of the Intrahepatic Biliary Tract, South African J. M. Sc. **15**:51, 1950.

8. Elias, H., and Petty, D.: Gross Anatomy of the Blood Vessels and Ducts Within the Human Liver, Am. J. Anat. **90**:59, 1952.

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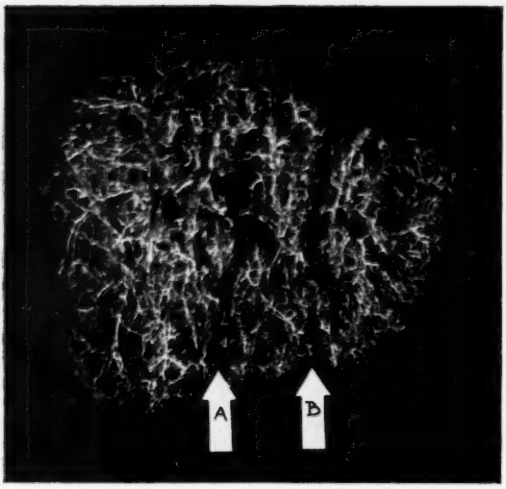

Fig. 1.—Vinyl acetate cast of the liver, as shown from the parietal surface, illustrating (*A*) the lobar fissure and (*B*) the left segmental fissure (bile ducts, in white; hepatic arteries, in red, and the portal vein, in blue).

Before describing the hepatic duct branching, it seems advisable first to give a brief account of our concept of the divisions of the liver. These divisions are based entirely upon the biliary drainage of this organ. The prevailing pattern of branching of the bile ducts and the main variants which were observed will then be described.

It is customary in describing the liver to distinguish two lobes, a right and a left. In textbooks of anatomy the division into the two lobes is placed on the parietal surface at the attachment of the falciform ligament, the left sagittal fissure dividing the liver on the visceral surface. However, as Bradley [9a] so aptly stated, "The division of the liver as made by human anatomists is convenient, but should not be held as resting upon an embryologic or true morphologic basis." We noted on the examination of our casts, that the division into a right and a left lobe was made by a

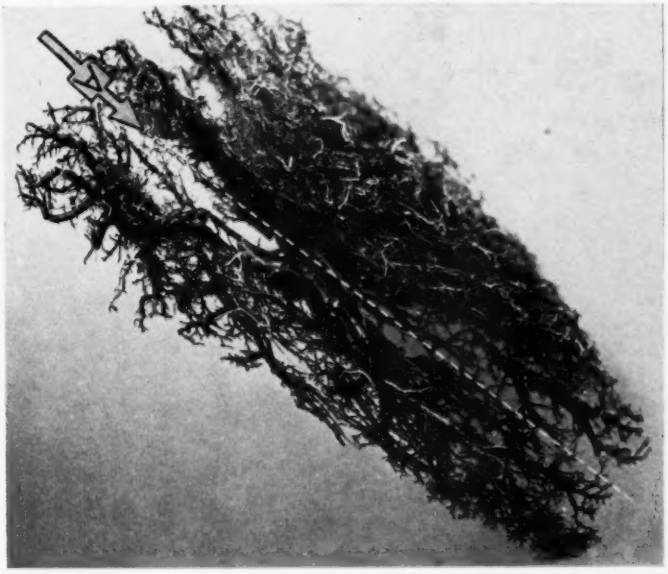

Fig. 2.—Photograph of a liver cast, showing right segmental fissure (indicated by arrow), as seen when right lobe is viewed from right side. It divides the right lobe into an anterior segment, which is to the right in the illustration, and a posterior segment, which is to the left.

fissure which we designated the lobar fissure. On the visceral surface of the liver this fissure followed a line through the gall-bladder fossa and the fossa for the inferior vena cava. Figure 1 depicts this fissure on the parietal surface. A division of this nature was first described by Cantlie in 1898. Hjortsjö called it "Hauptgrenzspalte" (main boundary fissure) and described its obliquity in detail. It should be clearly understood that there is no indication of the presence of this fissure on the parietal surface of the normal liver and that it can only be observed in casts in which the hepatic veins have not been injected. One of the main trunks of the hepatic veins (the middle) runs in this fissure within the liver substance. In the

9a. Bradley, O.: A Contribution to the Morphology and Development of the Mammalian Liver, J. Anat. & Physiol. **43**:1, 1909.

100 casts examined, however, no branches of the bile ducts, hepatic artery, or portal vein were seen to cross the fissure within the liver.

Each lobe was divided into two segments by fissures which could easily be seen in the casts. In viewing the casts from the right side, we noted that the right lobe was divided by an oblique fissure, the right segmental fissure (Fig. 2). It extended from the junction of the superior and posterior surfaces downward in an anterior direction and terminated just in front of the lower border of the liver. It was again a complete fissure extending into the porta hepatis and divided the right lobe into an anterior and a posterior segment.

A comparable fissure was present in the left lobe, the left segmental fissure (Fig. 1). It corresponded in position to the surface markings customarily used to

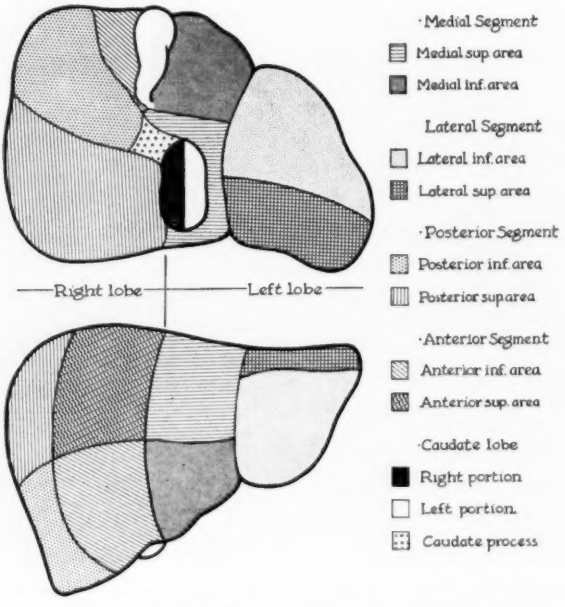

Fig. 3.—Divisions of the liver, as based upon the biliary drainage of this organ; visceral surface is shown in upper drawing, and parietal surface in lower drawing.

divide the liver into a right and a left lobe. Like the right segmental fissure, it extended into the porta hepatis. As evidenced in 20% of our specimens, however, small branches of the bile ducts and blood vessels may cross this left segmental fissure in the liver substance. The fissure divided the left lobe into a medial and a lateral segment. The medial segment corresponds in part to that portion of the liver called the quadrate lobe and formerly regarded as part of the right lobe. The lateral segment is coextensive with the left lobe, as used in the restricted sense.

Four segments of the liver may accordingly be defined on the basis of the biliary drainage, in the right lobe an anterior and a posterior segment, and in the left lobe a medial and a lateral segment. These segments, as will be shown shortly, are drained by the second order ducts (those of the first order being the main right and

left hepatic ducts). Each of the four segments may be subdivided in accord with their biliary drainage into two areas, a superior area and an inferior area (Fig. 3). These areas are drained by ducts of the third order.

In regard to the caudate lobe, we feel that it cannot be included entirely in either the right or the left lobe, as will be shown later.

Biliary Drainage of the Right Lobe.—The bile ducts draining the right lobe were examined in 97 casts. In each case, two main ducts drained this lobe; one came from the region of the anterior (ventral) segment, the other from the region of the posterior (dorsal) segment. These two ducts may therefore be termed the anterior and posterior segment ducts (Fig. 4).

The posterior segment duct is the longer of the two and usually somewhat superior in position. In each of the casts examined, this duct received the duct from the superior area of the posterior segment, and in 83 cases (86%) it received the

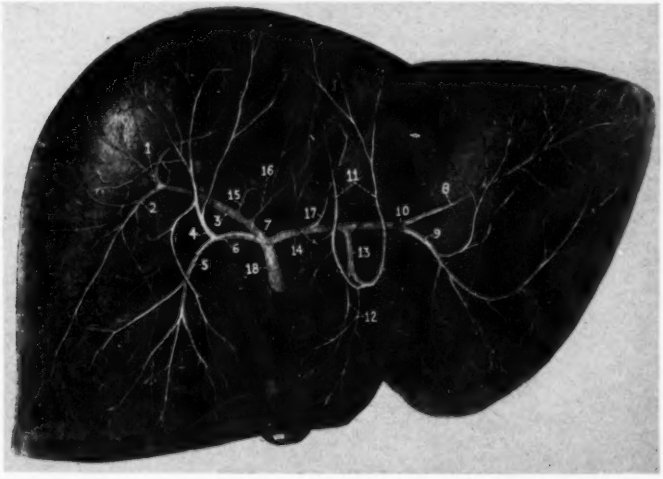

Fig. 4.—Composite drawing of prevailing pattern of branching of bile ducts in human liver, as seen from parietal surface. *1*, posterior-superior area duct; *2*, posterior-inferior area duct; *3*, posterior segment duct; *4*, anterior-superior area duct; *5*, anterior-inferior area duct; *6*, anterior segment duct; *7*, right hepatic duct; *8*, lateral-superior duct; *9*, lateral-inferior area duct; *10*, lateral segment duct; *11*, medial-superior area ducts; *12*, medial-inferior area ducts; *13*, medial segment duct; *14*, left hepatic duct; *15*, caudate process duct; *16*, right caudate duct; *17*, left caudate duct; *18*, common hepatic duct.

duct from the inferior area of the posterior segment (Fig. 4). Of the 14 cases in which the posterior-inferior area duct did not drain into the posterior segment duct, the drainage in 10 cases was into the anterior segment duct, in 2 into the right hepatic duct, and in 2 into the common hepatic duct (Fig. 5). In some specimens a small duct draining that part of the posterior-superior area adjacent to the caudate lobe emptied directly into the posterior segment duct instead of into the posterior-superior duct.

The anterior segment duct drained the superior area of the anterior segment in 78 cases (80%) and the inferior area of the anterior segment in 88 (91%). This is the prevailing pattern of the formation of this duct (Fig. 4). Aberrant

drainage of the anterior-superior area was noted in 19 cases (20%) and in each of these the duct from this area entered the posterior segment duct rather than the anterior one. Variations in the drainage of the bile ducts of the anterior-inferior area were seen in nine cases; in five of these the duct drained into the right hepatic duct and in four into the posterior segment (Fig. 5).

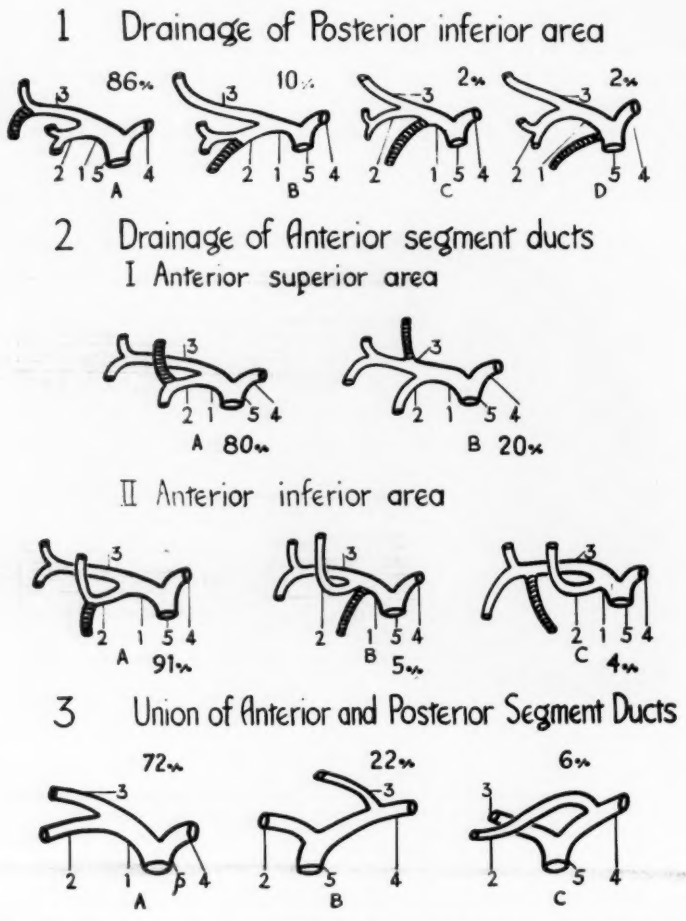

Fig. 5.—Diagram representing (1) prevailing pattern and variations of drainage of the duct of the posterior-inferior area; (2) prevailing pattern and variations of the ducts of the anterior segment, and (3) *A*, typical union of the anterior and posterior segment ducts to form the right hepatic duct, *B*, drainage of the posterior segment duct into the left hepatic duct, and *C*, drainage of the anterior segment duct into the left hepatic duct. *1*, right hepatic duct; *2*, anterior segment duct; *3*, posterior segment duct; *4*, left hepatic duct; *5*, common hepatic duct.

The anterior and posterior segment ducts extended medially to the region of the porta hepatis where the two joined to form the right hepatic duct (Fig. 4). This union of the two segment ducts occurred in 70 specimens (72%). In these cases

in which a true right hepatic duct was present, the duct averaged 9 mm. in length, with a range of from 2 to 25 mm. before joining the left hepatic duct to form the common hepatic duct.

In 27 cases (28%) the anterior and posterior segment ducts did not join to form a right hepatic duct. In 21 of these, the posterior segment duct extended to the left of the lobar fissure and entered the ducts of the left hepatic duct system (the left hepatic duct in 19, the superior duct of the lateral segment in 2). The left hepatic duct would then course to the right side of the porta hepatis and join the anterior segment duct of the right lobe to form the common hepatic duct. In six

Fig. 6.—Subvesical duct (*X*), located in the gall-bladder bed, is shown in this cholangiogram entering the anterior segment duct. Anterior and posterior segment ducts in this case do not unite to form the right hepatic duct.

instances, the anterior segment duct of the right lobe extended to the left of the lobar fissure to enter the left hepatic duct (Fig. 5).

In addition to the ducts of the right lobe previously mentioned, we have encountered an interesting and very important branch located in the gall-bladder bed (Fig. 6). This was found in 35 of the 97 casts in which the right lobe was examined, an incidence of 34.5%. In 16 of the 35 casts, this duct, which we have named the subvesical duct, drained into the anterior segment duct and in 11, into the right hepatic duct. Of the remaining casts, in four the duct entered the posterior-inferior area duct, in three into the anterior-inferior area duct, and in one into the left hepatic duct. One interesting feature of this duct was observed in casts in which

the portal vein was injected. Unlike other biliary ducts, the subvesical duct was not accompanied by a branch of the portal vein. In not a single instance did the subvesical duct have any direct communication with the gall bladder by so-called hepatocystic ducts in these casts.

Biliary Drainage of the Left Lobe.—As previously mentioned, the left lobe consists of a medial segment and a lateral segment separated by the left segmental

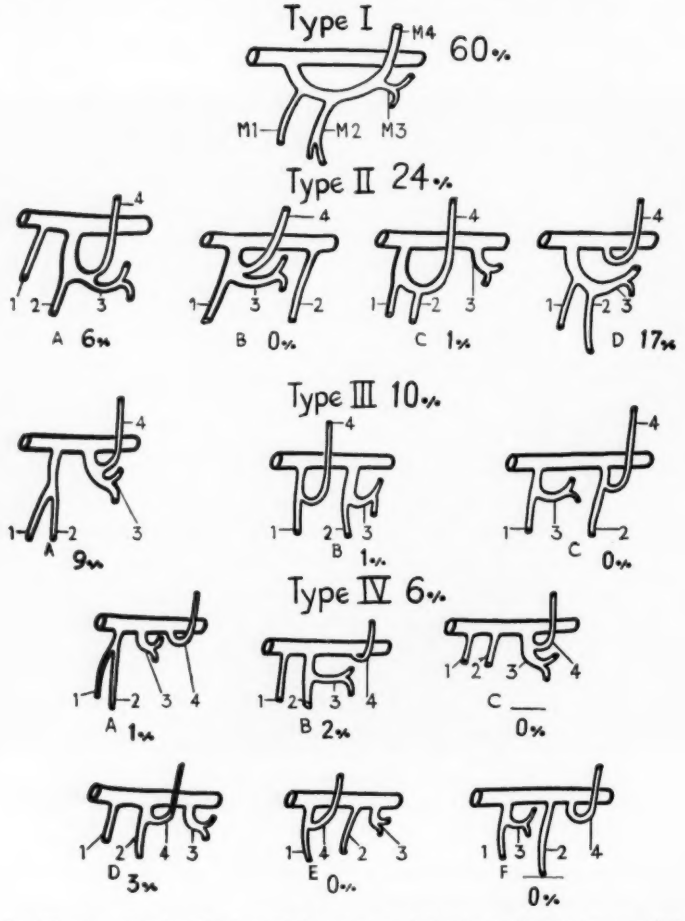

Fig. 7.—Diagram showing the four basic patterns of the ducts draining the medial segment of the left lobe. In addition to the actual combinations observed, the theoretical possibilities are also shown (*1* and *2*, medial-inferior ducts; *3* and *4*, medial-superior ducts).

fissure. The medial segment corresponds in part to the quadrate lobe and the lateral segment to the left lobe, as used in the gross descriptions of this organ. Here again, each segment is divided as to its biliary drainage into a superior and an inferior area.

The lateral segment is divided into a smaller superior area and a larger inferior area (Fig. 3). The duct of the inferior area was usually larger and longer than that

of the superior area and characteristically coursed through the lateral segment in an arc, the concavity of which faced upward (Fig. 4). It usually received the ducts draining the convex portion of the lateral segment, thereby accounting for the larger size of the inferior area. In six specimens, however, the ducts from the convex portion of the lateral segment emptied into the duct of the superior area. In these few cases therefore the superior area was the larger.

The superior duct of the lateral segment is usually the smaller of the two area ducts. It begins at the upper outer angle of the liver, at times (5%) extending into

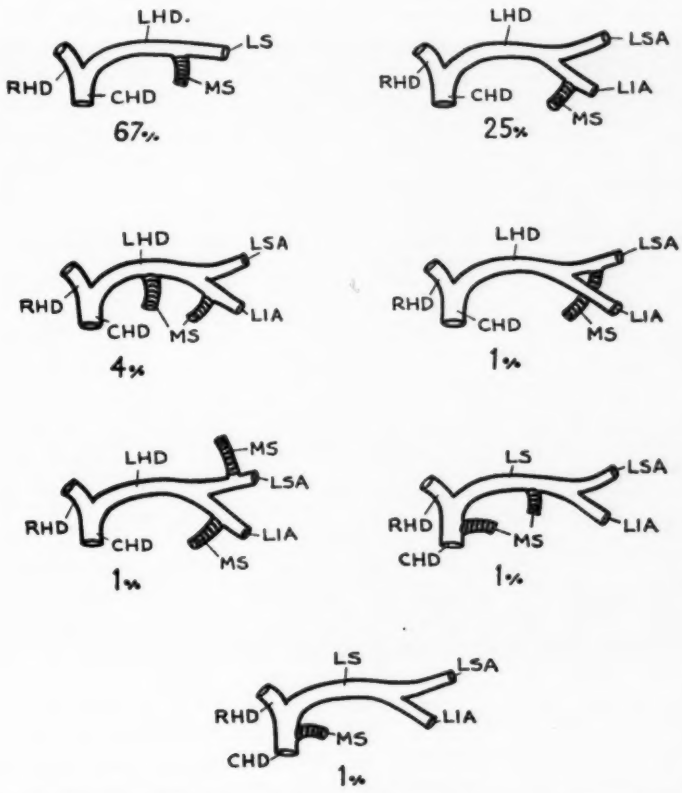

Fig. 8.—Variations in the sites of drainage of the medial segment duct. *CHD,* common hepatic duct; *RHD,* right hepatic duct; *LHD,* left hepatic duct; *LS,* lateral segment duct; *MS,* medial segment duct; *LSA,* lateral-superior area duct; *LIA,* lateral-inferior area duct.

the appendix fibrosa hepatis as a vas aberrans hepatis. From the periphery, the superior duct follows an oblique course downward toward the porta hepatis where it joins the inferior duct of the lateral segment to form the lateral segment duct (Fig. 4). The union of the two area ducts usually occurs in line with the left segmental fissure (50%), but in many cases (42%) it is placed to the right and less frequently (8%) to the left of the fissure.

The medial segment of the left lobe, as evidenced in our casts, comprises the remainder of the liver substance, with the exception of the caudate lobe. This medial

segment constitutes not only a portion of the visceral surface of the liver but includes all the area of the liver between the lobar fissure and the left segmental fissure; in other words, it comprises a portion of the parietal surface as well. Like the other segments, the medial segment may be divided in accord with its biliary drainage into a superior and an inferior area. The ducts draining the areas of the medial segment are more complex than those so far encountered. Instead of a single main duct draining the inferior area, as is the case in other segments, here there are two main ducts. Two ducts likewise drain the superior area (Fig. 4).

Four basic patterns of medial segment drainage were observed in our casts (Fig. 7). In Type I, the most prevalent (60%), all four of the area ducts joined to form a single medial segment duct. In Type II, one of the ducts (usually a superior duct) had a separate drainage, the remaining three ducts forming a single trunk (24%). In Type III, the two inferior ducts and the two superior ducts, respectively considered, usually formed a single trunk, each having a separate site of drainage (10%). In Type IV, two ducts drained separately and two by a common stem (6%).

TABLE 1.—*Correlation Between the Patterns and Sites of Drainage of the Medial Segment Duct*

Sites of Drainage	Pattern of Drainage				Total
	Type I	Type II	Type III	Type IV	
Lateral segment duct	47	12	4	4	67
Lateral-inferior duct	11	7	6	1	25
Lateral segment and lateral-inferior ducts	0	3	0	1	4
Lateral-superior duct	1	0	0	0	1
Lateral-superior and lateral-inferior ducts	0	1	0	0	1
Lateral segment and common hepatic ducts	0	1	0	0	1
Common hepatic duct	1	0	0	0	1
Total	60	24	10	6	100

In addition to the four patterns into which the area ducts of the medial segment may be categorized, there are also variations as to the site of drainage of the medial segment duct or ducts (Fig. 8). In most instances (67%), the medial segment duct joined the lateral segment duct to form the left hepatic duct (Fig. 4). This arrangement included ducts of all four basic patterns (Table 1). The medial segment duct, however, may enter the inferior or superior duct of the lateral segment. Drainage into the inferior duct was seen in 25% of the specimens, and in only one case did the medial segment duct drain into the lateral-superior duct. Such drainage was seen only if there was a late union of the ducts draining the lateral segment (Fig. 9). In not a single cast was the medial segment duct observed to cross to the left of the left segmental fissure to enter the ducts of the lateral segment.

The ducts of the medial segment may drain into sites other than those just described. Table 1 illustrates the correlation between the patterns and sites of drainage of the medial segment ducts. In two cases there was no union of the medial and lateral segment ducts of the left lobe (Fig. 8). In one of these the medial segment duct (Type I) emptied into the common hepatic duct. In the other case, a Type II pattern of drainage, the common trunk of the three ducts entered the common hepatic duct, while one of the superior ducts entered the lateral segment duct.

Aside from the drainage of the medial segment just described, there may be inconstant branches draining this segment. In 50 casts in which such branches were observed they all drained a small area of the medial segment just anterior to the caudate lobe and to the right of the fossa for the ligamentum venosum. Usually only one, at times two, of these branches were present; they were all of small caliber, and the majority of them drained into the lateral segment duct.

Worthy of note is the fact that the medial segment duct at times received branches from the region of the lateral segment which had crossed the left segmental fissure. These branches came from the convex portion of the lateral segment,

Fig. 9.—Cholangiogram illustrating a case in which there is a late union of the lateral-superior and lateral-inferior area ducts. Medial segment duct (*X*) drains into the inferior duct of the lateral segment in this specimen. Note also that the left caudate duct enters the superior duct.

a region usually drained by the inferior duct of that segment. Such branches were seen in 20 casts.

The lateral segment duct extended medially to join the medial segment duct and formed the left hepatic duct in 67 cases. The latter extended from the point of union of these two ducts to the common hepatic duct and had an average length of 1.7 cm. In 31 cases an atypical union of the two segment ducts of the left lobe was observed, i. e., the medial segment duct drained into the superior or inferior duct of the lateral segment. The question then arose as to what constitutes the left hepatic duct in these cases, since the late union of the superior and inferior ducts of the lateral segment should theoretically form the lateral segment duct. We maintain that since the biliary drainage of both the medial and the lateral segment is

included in these two area ducts their late union will form the left hepatic duct (Fig. 9). Accordingly, in these cases no lateral segment duct was present, it being included in the left hepatic duct. In two cases (2%) no left hepatic duct was formed, since no union of the medial and lateral segment ducts took place.

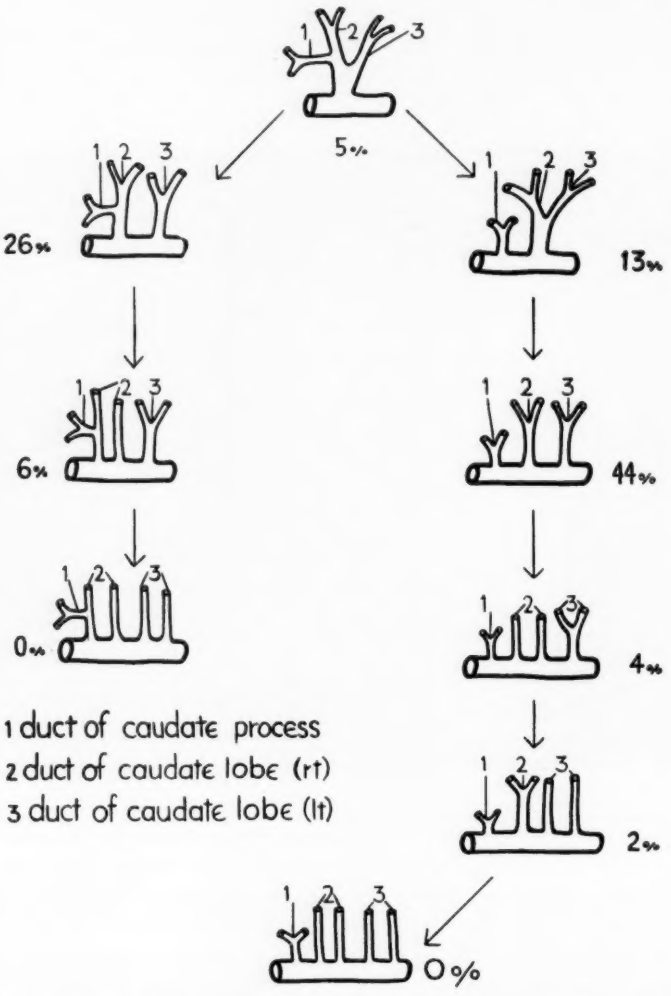

Fig. 10.—Actual and possible patterns of the ducts draining the caudate lobe.

Biliary Drainage of the Caudate Lobe.—The caudate lobe is situated on the posterior surface of the liver between the fossa for the inferior vena cava and the fossa for the ligamentum venosum. It may be divided into a caudate lobe proper, which is that part lying in the above position, and a caudate process. The latter consists of hepatic parenchyma connecting the caudate lobe to the right lobe of the

liver and is located between the porta hepatis below and the fossa for the inferior vena cava above. On the basis of its biliary drainage seen in our casts, we have come to the conclusion that the entire caudate lobe cannot be classified as belonging to either the right or the left lobe exclusively.

According to its drainage, the lobe may be divided into three parts: (*a*) the caudate process, (*b*) the right portion of the caudate lobe, and (*c*) the left portion of the caudate lobe (Fig. 3). Prevailingly, three ducts drained this caudate lobe, one from each of the three parts just described (Fig. 4). This pattern was observed in 44% of our specimens. In 26%, the duct draining the caudate process and the duct draining the right portion of the caudate lobe proper merged into a common duct; the duct draining the left portion of the caudate lobe remained separate. As illustrated in Figure 10, from one to four ducts may drain the caudate lobe.

The ducts draining the caudate lobe are markedly varied with regard to their sites of drainage. Theoretically, they may drain into the right or left hepatic duct systems or into both. In 78% drainage of the entire caudate lobe was into both the right and the left hepatic duct system (Fig. 4). The caudate ducts drained entirely into the left hepatic duct or its tributaries in 15%, and in 7% into the right hepatic

TABLE 2.—*Sites of Drainage of the Caudate Lobe Ducts*

Sites of Drainage	Caudate Process Duct	Right Caudate Duct	Left Caudate Duct
Anterior segment duct	0	1	0
Posterior segment duct	78	42	6
Right hepatic duct	7	9	1
Left hepatic duct	13	39	55
Lateral segment duct *	1	5	22
Lateral-superior duct *	1	4	16

* In the interpretation of these findings, it should be noted that the cases in which the caudate process duct or the right caudate duct enters either the lateral segment duct or the superior duct of the lateral segment are usually instances in which there is a late union of the area ducts of the lateral segment (Fig. 9).

duct system. More specifically considered, the duct of the caudate process usually (85%) drained into the right hepatic duct system and the duct of the left portion of the caudate lobe proper, in most instances (93%), drained into the left hepatic duct system. Since the right portion of the caudate lobe is intermediate in position, its ducts could enter into either the right or the left duct system. In our casts such drainage occurred in nearly equal frequency (into the right ducts 52% and into the left ducts 48%). Table 2 depicts the more specific sites of drainage of the individual ducts of the caudate lobe.

COMMENT

Biliary Drainage of the Right Lobe.—In our description of the segments of the right lobe, we distinguished two segments (anterior and posterior) in contrast to Hjortsjö [5b] who described three segments. He distinguished a dorsocaudal segment (our posterior), an intermediate, and a ventrocranial segment. The latter two are included in our anterior segment. As previously mentioned, our segment ducts are the second order of branching (the first order being the right and left hepatic ducts), and our area ducts are the third order ducts. The ducts draining that region of the right lobe which Hjortsjö called the ventrocranial segment are actually ducts of the fourth order (branches of either the anterior-inferior or the anterior-superior area

ducts) and therefore, in our opinion, the region drained by them should not be considered as a separate segment. He described the right hepatic duct, however, as being formed by two tributaries, which would be equivalent to our anterior and posterior segment ducts.

Fainsinger [7] described varying modes of formation of the right hepatic duct, the latter being regarded as bifurcating, trifurcating, or undergoing two successive bifurcations. Many of his observations were made from cholangiograms without the aid of corrosion specimens. Because of the overlapping of the anterior and posterior segment ducts in many cholangiograms, the interpretation of the formation of the right hepatic duct by this method alone in such a limited series of specimens is very difficult and likely to be erroneous.

In the literature a great variety of so-called accessory hepatic ducts have been described as occurring predominantly on the right side. In reality, these are simply cases in which no union of the anterior or posterior segment ducts have taken place or represent cases in which there was an aberrant drainage of the area ducts into the extrahepatic biliary tract (Fig. 5). Such a discrepancy is easily understood, since the cases described as "accessory" hepatic ducts were all based upon extrahepatic dissections of the bile ducts, the intrahepatic distribution being overlooked. By definition, accessory means an article that adds to the convenience or effectiveness of something else but is not essential. Since these ducts are segment ducts or rami of them—therefore essential—they should not be labeled as accessory, but rather as aberrant segment or area ducts.

The incidence of the latter (28%), as observed in our series, is considerably higher than the incidence of accessory bile ducts on the right side, as cited in the literature. Flint [10] found 29 in 200 dissections (15%), Michels [11] encountered 36 in the same number of specimens (18%), while Moosman and Coller [12] described 39 in 250 bodies examined (16%). These comparatively lower percentages may be accounted for, however, by the superiority of the corrosion method over that of gross dissection, which, in view of the depth of the porta hepatis, is rarely complete.

The presence of the subvesical duct that lies superficially in the gall-bladder bed warrants surgical care and consideration, as first emphasized by Haberland.[13] We found it to be present in about one-third of the casts (35%). In view of the incidence of this duct, removal of the gall bladder should always be accomplished with care and circumspection lest the duct inadvertently be torn, causing disconcerting postoperative leakage of bile.

Biliary Drainage of the Left Lobe.—Previous investigators [14] are in accord in their descriptions of the two main ducts of the lateral segment, differing only in the terminology used. The superior and inferior ducts draining the lateral segment of the left lobe showed little variation in their prevailing pattern, except as regards the

10. Flint, E.: Abnormalities of the Right Hepatic, Cystic, and Gastro-Duodenal Arteries and of the Bile Ducts, Brit. J. Surg. **10**:509, 1923.

11. Michels, N.: The Hepatic, Cystic, and Retroduodenal Arteries and Their Relations to the Biliary Ducts, with Samples of Entire Celiacal Blood Supply, Ann. Surg. **133**:503, 1951.

12. Moosman, D., and Coller, F.: Prevention of Traumatic Injury to the Bile Ducts, Am. J. Surg. **82**:132, 1951.

13. Haberland, H.: Studien an den Gallenwegen: V. Studien über die chirurgische Anatomie des Gallensystems, Arch. Klin. Chir. **139**:319, 1926.

14. Rex.[1] Melnikoff.[2] Hjortsjö.[5a] Fainsinger.[7]

late union of the two area ducts previously mentioned. Hjortsjö described the two areas as separate segments, designating the superior area, the dorsolateral segment, and the inferior area, the ventrolateral segment. The ducts draining these regions, however, are third order ducts, whereas, in our work, we maintain that segments of the liver are drained by second order ducts.

Reference may again be made to that portion of the lateral-superior duct that occasionally (5%) extended into the appendix fibrosa as a vas aberrans hepatis. Bile ducts in such a position were first described by Ferrein [15] in 1753. Most authors consider the vasa aberrantia as true biliary channels that are left superficial in position following the atrophy of the hepatic parenchyma which was originally related to them. The cause for this regressive process is unknown. Even though the hepatic cells gradually disappear, the bile ducts may not degenerate; in fact, they may undergo hypertrophy. Although these ducts are apparently functionless,[3] their continuity with the superior duct of the lateral segment may be of surgical importance owing to their relation to the left triangular ligament. Frequently, during such an operative procedure as a total gastric resection, the left triangular ligament is incised in order to gain a more adequate exposure. The possible presence of the terminal end of the lateral-superior duct in relation to this ligament should then be kept in mind.

In view of the mode in which the biliary drainage of the medial segment of the left lobe of the liver actually takes place, we suggest that the term "quadrate lobe" be regarded as pertaining to the liver tissue which is coextensive with the medial segment, or that the term be discarded entirely. The textbook term "quadrate lobe" refers only to an area—not a true lobe—on the visceral surface of the liver, which, in the majority of cases, is not quadrate in shape.

The left hepatic duct has always been regarded as extending from the common hepatic duct to what would be the point of union of our superior and inferior ducts of the lateral segment. We hold that this is true in cases of late union of these two area ducts. Prevailingly, however, the left hepatic duct, as evidenced in our casts, extends from the common hepatic duct to a point where the medial segment duct joins the lateral segment duct.

The two cases in which there was no union of the medial and lateral segment ducts, i. e., cases in which no true left hepatic duct was observed, are comparable to the cases described on the right side in which there was no union of the anterior and posterior segment ducts. These two cases in an extrahepatic dissection would ordinarily be classified as "accessory" left hepatic ducts. The claim is sometimes made that "accessory" hepatic ducts do not occur on the left side, although Moosman and Coller [12] found 1 in 250 cases (0.4%). Here again, as on the right side, we claim these are not "accessory" hepatic ducts but rather aberrant segment ducts.

Biliary Drainage of the Caudate Lobe.—Despite the fact that in our casts the ducts from the caudate lobe predominantly (78%) emptied into both the right and the left hepatic duct system, we never observed any communication between these two duct systems in the region of the caudate lobe, as stated by Kiernan [16] and Long-

15. Ferrein, A., cited by Poirier, P., and Charpy, A.: Traité d'anatomie, Paris, Masson et Cie, 1912, Vol. 4, p. 769.

16. Kiernan, P.: The Anatomy and Physiology of the Liver, Philosophical Tr. Roy. Soc., London **133**:711, 1883.

mire.[17] McIndoe and Counsellor [3] also denied the existence of a communication between the right and left hepatic ducts and emphasized the fact that the slight transfer of dyes that may occur between these two systems after injection takes place via a vestigial structure, the vasa aberrantia, located in the cleft between the right and left hepatic ducts. Our findings are also in accord with those of Stewart, Cantarow, and Morgan,[18] who, in experiments upon cats, were unable to find any evidence of anastomoses between the right and left hepatic ducts in cases of partial obstruction. Schalm,[19] in recent experimental ligation studies, came to the conclusion that no functional anastomoses occur between the right and left duct systems even after prolonged obstruction and offered clinical evidence to substantiate his findings.

CLINICAL SIGNIFICANCE

There is a striking similarity between the liver and the lung when certain of their anatomic features are considered. Developmentally, both organs arise as entodermal diverticula giving rise to central tubular structures (the bronchial and biliary trees) that grow into mesodermal tissue. Each organ receives two sets of afferent blood vessels, one nutritive (bronchial arteries and hepatic arteries), the other functional (pulmonary artery and portal vein). Both have a single set of efferent channels (pulmonary veins and hepatic veins), and although the external morphology and histologic aspects of both the lung and the liver were well known for many years, the intrapulmonary and intrahepatic gross anatomy have only recently been emphasized from a practical viewpoint. New advances in the fields of pathology, roentgenology, and surgery make it imperative that we possess a knowledge not only of the prevailing pattern and variants of the branching of the bronchial tree but also of the biliary passageways.

The concept of a segmental drainage of the bile ducts may be of practical significance. Certain segments of the liver may be affected by a particular pathologic lesion more so than others, as is the case in pathologic lesions of the lung where they may be confined to one or more of the segments. Investigations have already been made with regard to the selective involvement of the lobes of the liver by certain diseases. Glénard [20] was the first to come to this conclusion on the basis of clinical observations. He suggested that certain diseases affect the right lobe, others the left lobe, an observation confirmed by other investigators. Whether certain segments of the liver are subject to similar predilection by disease, remains to be determined. Likewise to be solved is the role which the blood supply plays in this process.

A knowledge of the intrahepatic segmental arrangement of the biliary passageways is extremely important to the roentgenologist. Since first popularized as a roentgenologic method by Mirizzi [21] in 1932, cholangiography is being utilized with

17. Longmire, W., and Sanford, M.: Intrahepatic Cholangiojejunostomy with Partial Hepatectomy for Biliary Obstruction, Surgery **24**:264, 1948.

18. Stewart, H.; Cantarow, A., and Morgan, D.: Changes in the Liver of the Cat Following Ligation of Single Hepatic Ducts, Arch. Path. **23**:641, 1923.

19. Schalm, L.: The Use of the Regenerative Power and Reserve Capacity of the Liver in Bile Duct Operations, Arch. chir. neerl. **3**:322, 1951.

20. Glénard, F.: Des résultats objectifs de l'exploration du foie chez des diabetiques, Lyon méd. **44**:5, 1890.

21. Mirizzi, P.: La Cholangiographia durante las operaciones de las vias biliares, Bol. y trab. Soc. cir. Buenos Aires, **16**:1133, 1932.

increasing frequency. The technique now employed requires a laparotomy and has therefore been used primarily for the localization of stones in the biliary duct system at operation or during the postoperative period. According to Fainsinger, attempts are being made to overcome this objection of an operative procedure, i. e., laparotomy, by such methods as retrograde cholangiography, injection of the gall bladder under peritoneoscopic control, or by blind puncture of the gall bladder. Improvement of such methods may allow cholangiography to become very useful in the diagnosis of various liver diseases, such as congenital anomalies of the ducts, fibrotic conditions of the liver causing narrowing or tortuosity of the ducts, or tumor

Fig. 11.—Cholangiogram illustrating a great displacement of the ducts of the right lobe, especially the posterior-superior duct (compare with Figs. 6 and 9). This liver was found to have a large metastatic carcinomatous mass located in the posterior-superior area of the right lobe. This also shows the posterior segment duct (*X*) emptying into the lateral-superior duct.

formation causing bile duct displacement (Fig. 11). Again, as shown in the early experiences with bronchography, one must first possess a knowledge of the normal anatomic patterns in order to interpret abnormal roentgen findings.

A knowledge of the intrahepatic anatomy of the bile ducts is becoming increasingly important to the surgeon. At present, diverse attempts are being made to correct strictures of the bile ducts in a more radical manner. This is especially true in those cases in which it is impossible to obtain a common hepatic duct of sufficient length for use in a reconstructive procedure. In such cases, intrahepatic cholangiojejunostomy with partial hepatectomy, as first described by Longmire [17] or as

modified by others,[22] is being utilized. Partial hepatectomies are also being performed in cases with solitary metastatic carcinomatous lesions, especially in the lateral segment. These operative procedures are hazardous, for they have no anatomic basis. We are at the same stage in hepatic surgery today that we were in pulmonary surgery before the individual ligation technique of pulmonary resection was introduced. We have no true knowledge of the topographic relationship of the intrahepatic bile ducts and the intrahepatic blood vessels, for they have not been sufficiently studied in the past. In a subsequent paper we hope to give our observations of these topics as ascertained in liver casts.

SUMMARY

The liver is divided into a right and a left lobe by the lobar fissure that is roughly in line with the gall-bladder bed and the inferior vena cava on the visceral surface.

The right lobe is divided by the right segmental fissure into two segments, one anterior, the other posterior.

The left lobe is divided into a medial and a lateral segment by the left segmental fissure that is in line with the umbilical fossa and the fossa for the ligamentum venosum.

Each segment may be divided in accord with its biliary drainage into a superior and an inferior area.

The prevailing pattern of drainage of these areas and segments is presented, as well as the major variants observed.

The so-called accessory hepatic ducts are actually not accessory but aberrant segmental or area ducts.

The quadrate lobe comprises not only a portion of the visceral surface of the liver, as stated in textbooks, but should be regarded as pertaining to liver tissue that is coextensive with the medial segment.

The subvesical duct located in the gall-bladder bed is described and its surgical significance presented.

No communication between the right and the left hepatic duct system was observed in these casts.

22. Cole, W.; Ireneus, C., and Reynolds, J.: Strictures of the Common Duct, Ann. Surg. **133**:684, 1951. Zavaleta, D.: Hepatostomiá interna, Bol. y trab. Acad. argent. cir. trab. **35**: 685, 1951.

USE OF CRYSTALLINE SOYBEAN TRYPSIN INHIBITOR IN ACUTE HEMORRHAGIC PANCREATITIS IN DOGS

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THE ISOLATION of crystalline soybean trypsin inhibitor by Kunitz[1] in 1946 suggested the use of this material in the treatment of acute hemorrhagic pancreatitis.

Coffee, Brinig, and Gillespie,[2] in 1950, while studying the abnormal tryptic activity of the blood in acute pancreatic necrosis, reported that the antitryptic index of the blood serum, carried out by the gelatin-digestion method, was significantly lowered both in experimental and in clinical pancreatic necrosis. In contrast, there was no change from the normal levels in pancreatic edema. The antitryptic index could be depressed by the use of crystalline soybean trypsin inhibitor. In this work, the antitrypsin appeared to protect small animals against toxic doses of trypsin and to modify the course of experimentally produced pancreatic peritonitis.

Rush and Cliffton,[3] in 1951, in experiments on 12 dogs used soybean trypsin inhibitor in 3 of these animals with experimentally produced pancreatitis and concluded that the soybean trypsin inhibitor was capable of specifically counteracting the elevation of proteolytic activity and shock found in acute pancreatitis. They concluded that the soybean trypsin inhibitor might have considerable potential value in the clinical treatment of the shock of acute hemorrhagic pancreatitis.

Our experiments were started before the publication of Rush and Cliffton's report, with the idea of evaluating the use of soybean trypsin inhibitor on the mortality rate in dogs with experimentally produced acute hemorrhagic pancreatitis. The possible use of soybean trypsin inhibitor in the clinical treatment of acute pancreatitis was the ultimate goal in mind.

The technical assistance of Miss Kay Fowler is acknowledged.

From the Katz-Sanders Surgical Research Laboratory, Mt. Sinai Hospital.

1. Kunitz, M.: Crystalline Soybean Trypsin Inhibitor: General Properties, J. Gen. Physiol. **30**:291, 1947.

2. Coffee, R. J.; Brinig, F. J., and Gillespie, J.: Trypsin and Antitrypsin in Acute Pancreatic Disease, in Forum on Fundamental Surgical Problems: Surgical Forum, 1950; Proceedings of the Forum Sessions of the Thirty-Sixth Clinical Congress of the American College of Surgeons, edited by O. Wangensteen, Philadelphia, W. B. Saunders Company, 1951, p. 166.

3. Rush, B., Jr., and Cliffton, E. E.: Role of Trypsin in the Pathogenesis of Acute Hemorrhagic Pancreatitis and the Effect of Antitryptic Agent in Treatment, Surgery **31**:349, 1952.

EXPERIMENTAL METHOD

A total of 91 healthy mongrel dogs were used in these experiments, ranging in weight from 19 to 40 lb. (8.6 to 18.1 kg.) and fed on standard kennel rations. No supportive therapy was given to any of the animals postoperatively. They were allowed to eat and drink at will. Thiopental (nembutal®) sodium (5%) given intravenously was used as the anesthetic agent in all dogs. In dogs that had been fed up to experiment time, pancreatitis was produced by isolation, cannulization, and injection of bile into the main pancreatic duct after midline laparotomy under sterile conditions. After injection of the bile, the pancreatic duct was ligated above and below the site of insertion of the plastic cannula.

Bile was obtained by aspiration of the gall bladder. This bile was injected into the pancreatic duct with a moderate amount of pressure in an effort to disrupt the smaller pancreatic ducts. The greatest amount of bile injected was 10 cc.; the smallest amount, 5 cc. The amounts used varied directly with the size of the dog. After laparotomy, most of the dogs were given a powdered milk solution by way of a stomach tube.

TREATMENT

Sixty-one dogs were treated with crystalline soybean trypsin inhibitor. Thirty dogs were used as controls. Pure crystalline soybean trypsin inhibitor [4] was used in all animals. The dosage schedules used in treatment were as follows:

Group I (29 dogs). Forty milligrams of soybean trypsin inhibitor was administered intravenously every 4 hours for 24 hours starting 4 hours after operation. The total dose for each dog was 240 mg.

Group II (19 dogs). One hundred milligrams of soybean trypsin inhibitor was administered intravenously every 4 hours for 24 hours starting 4 hours after operation. The total dose for each dog was 600 mg.

Group III (10 dogs). Two hundred and fifty milligrams of soybean trypsin inhibitor was administered intravenously immediately after laparotomy. Two hours later 250 mg. was given intravenously and then 100 mg. intravenously every 4½ hours for five times. The total dose for each dog was 1,000 mg.

Group IV (3 dogs). The treatment schedule was the same as in Group III, except that the soybean trypsin inhibitor was given intraperitoneally.

LABORATORY DETERMINATIONS

Daily serum amylase determinations by a modified Somogyi [5] method were made on all animals as long as they lived or until a plateau was reached. Daily serum lipase determinations on the last 23 dogs used were done by the method of Loevenhart [6] (modified by Johnson and Bockus). Daily serum trypsin levels were done by Kunitz' method (casein digestion) on all animals as long as they lived or until the level remained constant. This method indirectly shows the effect of the antitrypsin by measuring the tryptic activity. This method is as follows:

A 0.01% trypsin (Worthington Biochemical Laboratory) solution is made up in a phosphate buffer of pH 7.8. A 1% casein (isoelectric difco®) solution is made up in a phosphate buffer of pH 7.8.

4. Pure crystalline soybean trypsin inhibitor was supplied by Worthington Biochemical Laboratory, Freehold, N. J.

5. Somogyi, M.: Blood Diastase as Indicator of Liver Function, Proc. Soc. Exper. Biol. & Med. **32**:538, 1934.

6. Gradwohl, R. B. H., and Kouri, P.: Clinical Laboratory Methods and Diagnosis: A Textbook on Laboratory Procedures with Their Interpretation, Ed. 4, St. Louis, C. V. Mosby Company, 1948, Vol. 1, p. 395.

Serum from an unknown (experimental) animal is diluted 1 to 50. Into a test tube are put 1 cc. of the 1 to 50 dilution of serum, 1 cc. of the trypsin solution, and 3 cc. of the phosphate buffer solution. This mixture is heated to 40 C. in a water bath and allowed to stand 10 minutes. In this same water bath there is a control tube of 1 cc. of 0.01% trypsin solution and 4 cc. of phosphate buffer. This is allowed to stand for 10 minutes.

At 30-second intervals, 2 cc. of the 1% casein solution is added to each tube and allowed to stand for 15 minutes in the water bath. At the end of 15 minutes, at 30-second intervals, these tubes are transferred to an ice bath in the same order as they were treated, adding at the time of transfer 3 cc. of 5% trichloroacetic acid and shaking well. When thoroughly chilled, each tube is filtered. Each filtrate is centrifuged for 20 minutes at 3,000 rpm. The supernatant fluid is poured off and read in the Beckman DU spectrophotometer at 280μ, using the phosphate buffer

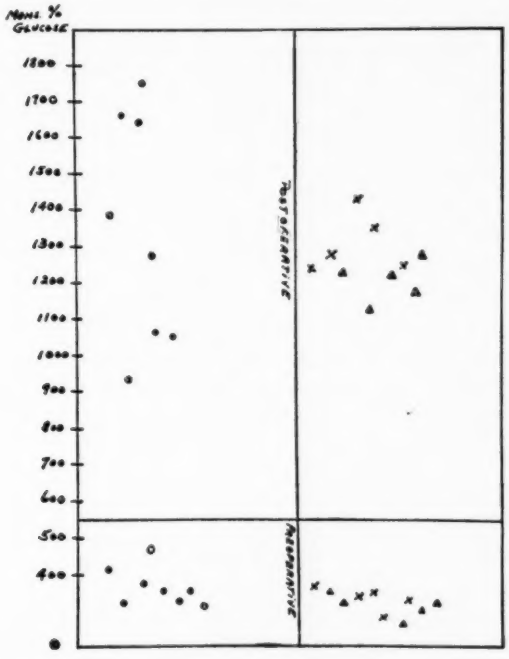

Chart 1.—Amylase determinations. Black dot represents untreated animals that lived; circle, untreated animals that died; x, treated animals that lived, and triangle, treated animals that died.

for determining the zero point. The reading of the test sample is subtracted from that of the control.

Autopsy was performed on all animals that died, and tissue sections were made of the pancreas and any areas of fat necrosis. In those animals that survived formal biopsy specimens of the pancreas were taken at varying intervals after seven days. These were obtained through repeat laparotomy.

POSTMORTEM AND TISSUE STUDIES

Autopsies were done on all dogs that died. The findings were typical, varying somewhat with the time of death. Bloody fluid was present in the peritoneal cavity. The pancreas showed varying degrees of hemorrhagic infiltration and necrosis. Fat

necrosis was present. Tissue sections showed the typical picture of acute hemorrhagic pancreatitis. In formal biopsies of the pancreas in dogs that survived, the tissue sections showed extensive scarring and fibrosis. Grossly, the pancreas was small, hard, and fibrotic. No difference was noted in any instances between treated and untreated dogs as regards autopsy findings or tissue sections.

RESULTS

Serum Amylase Studies.—All dogs, whether treated or untreated, showed the typical elevation of the serum amylase level, usually within a few hours.

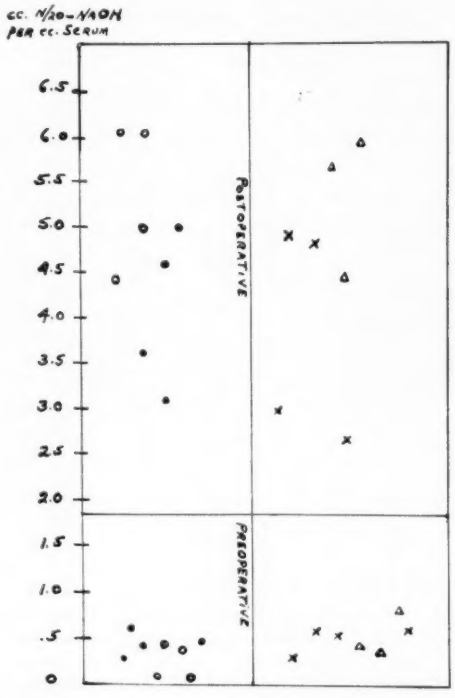

Chart 2.—Lipase determinations. Black dot represents untreated animals that lived; circle, untreated animals that died; x, treated animals that lived, and triangle, treated animals that died.

Chart 1 shows representative preoperative and postoperative serum amylase levels in both treated and untreated animals. The postoperative readings represent the highest level obtained when the animal survived 24 hours or more.

The use of soybean trypsin inhibitor had no influence on serum amylase levels.

Serum Lipase Studies (23 Dogs).—All dogs studied showed a typical rise in serum lipase levels, which were not affected by the use of soybean trypsin inhibitor.

Chart 2 shows representative preoperative and postoperative serum lipase levels in both treated and untreated animals. The postoperative readings represent the highest level obtained when the animal survived 24 hours or more.

Trypsin Studies.—Here again we could not demonstrate any direct effect of the use of soybean trypsin inhibitor. We do not find any constant trend in the treated dogs. Trypsin levels increased or decreased without any apparent relation to the use of the soybean trypsin inhibitor. If the soybean trypsin inhibitor had been effective, the trypsin levels should have decreased in treated dogs, especially if they survived.

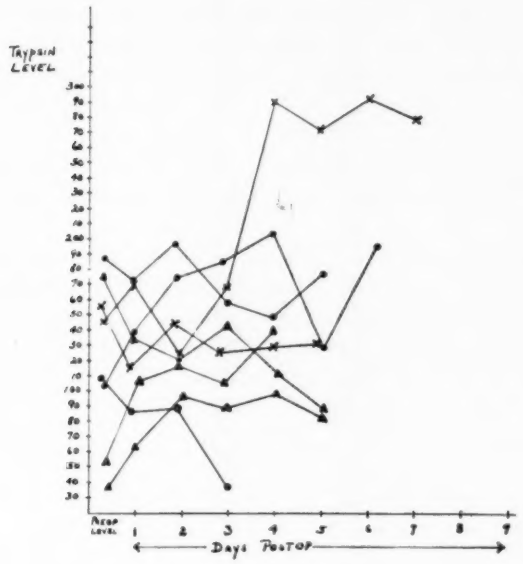

Chart 3.—Sample trypsin curves. Black dot represents untreated animals that lived; circle, untreated animals that died; x, treated animals that lived, and triangle, treated animals that died.

Table 1 shows the preoperative and 24-hour postoperative trypsin levels in the treated, as well as in the untreated, group of dogs. There was no constant relationship between the 24-hour postoperative trypsin level and the end-result of the experiment.

In our untreated group there was a 50% mortality rate. In the treated group the mortality rate varied slightly with the method of treatment, but the over-all mortality rate was 50.8%. The dogs that died in the treated group did not survive any longer than those that died in the untreated group. The trypsin titers of the dogs dying in the treated group showed no constant trend. Some titers increased and some decreased.

TABLE 1.—*Trypsin Levels*

Animals	Preoperative Trypsin Levels	Postoperative Trypsin Levels	No. of Dogs with Increased Trypsin Levels	No. of Dogs with Decreased Trypsin Levels
Treated and lived	145	170	15	11
	191	184		
	191	206		
	178	157		
	143	159		
	129	210		
	187	264		
	190	193		
	117	151		
	147	145		
	166	173		
	116	121		
	149	180		
	140	128		
	131	100		
	121	120		
	137	91		
	151	111		
	176	183		
	137	183		
	182	174		
	170	182		
	57	81		
	72	51		
	44	80		
	41	26		
Treated and died	162	212	6	10
	180	184		
	195	145		
	124	135		
	144	112		
	133	120		
	133	166		
	286	165		
	130	133		
	150	126		
	174	133		
	188	153		
	183	156		
	81	54		
	66	81		
	70	30		
Untreated and lived	111	138	7	6
	153	140		
	216	248		
	198	291		
	189	170		
	122	125		
	120	140		
	118	123		
	125	139		
	75	73		
	100	45		
	61	60		
	94	76		
Untreated and died	141	128	5	1
	105	125		
	82	101		
	101	106		
	85	90		
	60	95		

TABLE 2.—*Mortality for Treated and Untreated Animals*

Animals	Died		Lived	
Untreated		15		15
Treated		31		30
Group I	15		14	
Group II	7		12	
Group III	7		3	
Group IV	2		1	

COMMENT

According to Kunitz, the reaction of soybean trypsin inhibitor and trypsin in the serum is an instantaneous one. Therefore we did expect to see some downward trend of the trypsin titers after the use of the inhibitor. Our work failed to show this. It is possible that our doses were not large enough and that the most marked liberation of trypsin is in the first few hours after the creation of the experimental pancreatitis.

In spite of this, we would expect some noticeable effect from the use of soybean trypsin inhibitor, especially since in our dosage schedule the last dose of soybean trypsin inhibitor was given shortly before the first 24-hour postoperative blood specimen was drawn. Our results do not bear this out.

Certainly, the mortality rate for the treated group shows no improvement over that for the nontreated group. One explanation is that it is possible that the mortality in acute hemorrhagic pancreatitis is caused by some substance or substances other than the trypsin per se.

SUMMARY

Experimental acute hemorrhagic pancreatitis was created in 91 dogs.

Thirty dogs were untreated and were used as controls—the mortality rate was 50%.

Sixty-one dogs were treated with pure crystalline soybean trypsin inhibitor in varying dosages. The mortality rate was 50.8%.

Crystalline soybean trypsin inhibitor was found to be ineffective in the treatment of experimental acute hemorrhagic pancreatitis in dogs under the condition of these experiments.

HOMOTRANSPLANTATION OF THE DOG HEART

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ONE OF the constant findings in a liverless dog is a progressive tachycardia. Consequently, 24 hours after hepatectomy the heart rate of the animal may be about 250 beats a minute. The animal otherwise may appear normal and walk about the room with little evidence to show that it has been subjected to a major operation. In an effort to elucidate the nature of this tachycardia my colleagues and I decided to connect the circulation of a liverless dog with that of a transplanted heart. If the transplant also shows tachycardia, one can be certain that this is a result of a humoral agency consequent upon removal of the liver. Because the technique of homotransplanting a heart turned out to be feasible, once we became familiar with it, we transplanted a series of 30 hearts, of which 23 survived. They beat on an average for 129 hours, and two hearts survived for 245 and 240 hours, respectively. The pulsations were regular and vigorous. Our experiences with this research form the subject of this paper. We presented a colored moving picture of the operation and the subsequent appearance of the dog to the Toronto Physiological Society, March 4, 1952.

One may reasonably ask why such a simple physiological problem should be investigated by what appears to be a round-about difficult technical procedure. We may answer by stating that the restoration of the heart beat in the cardiac transplant is almost as certain as in a rabbit heart perfused by Locke's solution. Instead of cannulating the aorta with the perfusion apparatus, we connect the aorta of the transplant to the common carotid artery, suturing this by the well-known Carrel method. Instead of the fluid that leaves the coronary circulation being caught in a funnel and returned to the reservoir, it is collected via the pulmonary artery, which is sutured to the external jugular vein. When the caval orifices and the pulmonary venous orifices are ligated, there is a closed system for the coronary perfusion of the excised heart (Fig. 1).

EXPERIMENTAL METHODS

Dogs weighing about 15 kg. with long necks and heavy jowls were most suitable because of the increased area present for the transplantation of the heart into the neck region and because the loose skin allowed the heart to be covered without undue pressure. The transplanted hearts were obtained from pups that weighed approximately 2,700 gm. and were 6 to 8 weeks of age.

Ether was used as the anesthetic for the host and pentobarbital (Nembutal) for the pup. We felt that pentobarbital was unsuitable for the host because the long period of postoperative recovery, with its attendant excitement, might damage the transplant. We need say nothing

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about the preparation of the blood vessels in the neck of the host, except to mention that we used ordinary technique for vascular anastomosis, 5-0 anacap® nonabsorbable surgical (silk) sutures being used. The suture material was wiped with a swab dipped in liquid petrolatum. The pup heart was removed by opening the thorax through a midline incision of the cariniform cartilage, using adequate artificial respiration. The mediastinum was then gently broken down to allow entrance to both sides of the thoracic cavity. The internal thoracic vessels were tied off on each side and cut between ligatures. The thymus gland was pulled up and forward, out of the thoracic cavity. The azygos vein was found, tied close to the anterior vena cava, and cut between ligatures. The anterior vena cava was then separated gently from the surrounding tissues and tied and cut between ligatures. The ligatures in this case were placed as close to the heart as possible. The brachiocephalic artery was found, and, if it appeared to be too large to be sewn to the carotid of the recipient, it was tied close to its emergence from the base of the heart and cut between ligatures. If it appeared to be the correct size, it was tied as far forward as possible and cut between ligatures. The ends of the ligature on the portion attached to the heart were left long for future handling. When the brachiocephalic

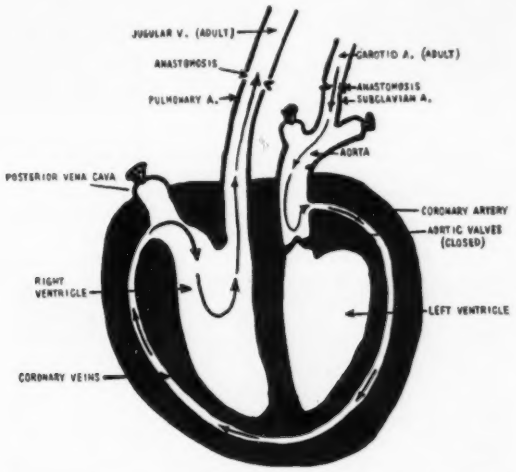

Fig. 1.—Diagrammatic representation of circulation through transplanted heart.

artery proved too large, the subclavian artery was selected. In a few cases the aorta of the pup heart was sutured directly to the comomn carotid of the host. (This is harder to do, as the aorta of a pup is friable and does not hold suture material easily.) The aorta was then exposed, and a loose ligature was slipped through the arch. The posterior vena cava was found and a loose ligature was placed around it close to the heart. One-half cubic centimeter of heparin (500 units) was then injected into the posterior vena cava between the ligatures and the diaphragm. Sufficient time was allowed for the heparin to make its way through the heart, and then the posterior vena cava was tied and cut between ligatures. The heart usually continued to beat for some time. After 30 or 40 seconds the aorta was tied tightly and cut between ligatures. The heart, with lungs attached, could now be removed from the thoracic cavity. It was placed on a moist towel, and the lung lobes were tied firmly and cut off individually. The pulmonary artery was then dissected free and a serrefine (bulldog) was placed over its cardiac end. The vessel was then cut with iris scissors as close to the lung stump as possible. The brachiocephalic or subclavian artery was stretched and treated in the same manner. The vessels were then prepared for blood vessel anastomosis in the usual manner, except that liquid petrolatum was not used because of fear of coronary embolism. Clots were washed out by means of isotonic saline. The heart was then transferred to the neck of the recipient dog, and the vessels to be

sewn were approximated. The pulmonary artery was sewn to the jugular vein and the subclavian artery to the carotid artery of the adult, as described by Markowitz [1] (1949).

When the sewing was completed, the serrefines on the jugular vein and the pulmonary were removed; then the serrefine on the carotid artery on the cardiac side of the anastomosis was released. This caused a slight amount of hemorrhage at the suture line. Air in the vessel next

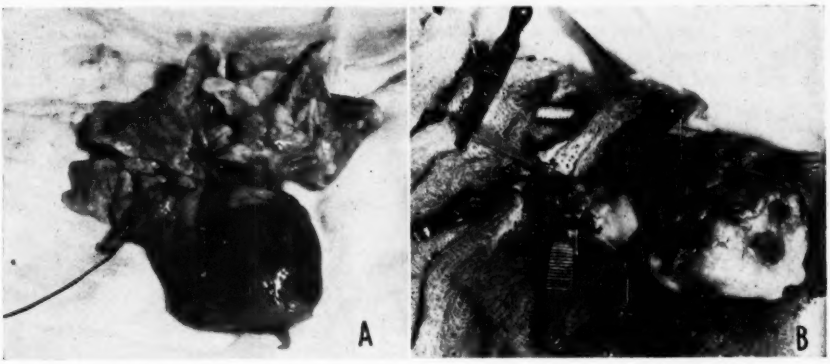

Fig. 2.—*A*, showing heart upon removal from chest of pup, with lungs still attached. Anterior vena cava, posterior vena cava, and vena azygos, and aorta and brachiocephalic and subclavian arteries have all been ligated. Ligature on subclavian artery was not cut and can be seen extending to left in photograph. *B*, showing same heart anastomosed to carotid and jugular arteries of adult dog. Carotid subclavian anastomosis is in foreground; pulmonary artery jugular anastomosis, in background.

Fig. 3.—Showing same heart as in Figure 2, 240 hours after transplantation. Heart had ceased to beat; host was anesthetized and skin incised over transplant. Fibrous tissue adhesions were broken away from pericardial sac, and organ was removed. In photograph fibrous tissue can be seen on pericardial sac and in neck region of dog. Arterial anastomosis is intact and can be seen above heart in region of incision.

to the remaining arterial bulldog forceps was quickly squeezed out through the suture line with the aid of the fingers. In the event that hemorrhage did not occur, it was encouraged, for the removal of this air is essential.

1. Markowitz, J.: Experimental Surgery, Including Surgical Physiology, Ed. 2, Baltimore, Williams & Wilkins Company, 1949.

On deciding that not even a tiny bubble of air remained in the pocket adjoining the suture line, the remaining bulldog forceps was removed. Atrial and ventricular contractions were initiated, usually in 30 or 40 seconds. Occasionally, fibrillation developed, and a careful inspection would usually disclose a bubble in one of the coronary vessels. The beat was fast and regular, and the expulsion of blood occurred through the jugular vein. The skin edges were

Typical Protocol

Date: June 29, 1951

Adult

Breed or Description: Mongrel terrier, female, mature
Initial Weight: 45 lb. (20 kg.)
Condition: Good — **Temperature:** 102.6 F.
Anesthesia: Ether

Pup

Breed or Description: Collie; male; age, 9 wk.
Initial Weight: 2,500 gm.
Condition: Good — **Temperature:** 101.8 F.
Anesthesia: Pentobarbital intraperitoneally

Medication

Adult: 300,000 I.U. penicillin daily for 3 days before operation
Pup: 300,000 I.U. penicillin daily for 3 days before operation
Postoperatively: 300,000 I.U. crystalline penicillin in wound
300,000 I.U. penicillin G in oil daily

Operation commenced at 9:00 a.m. Operation completed at 11:45 a.m.

Date	Time	Adult Heart Rate	Transplanted Heart Rate	Temperature, F.	Comments
6/29/51	1:00 p.m.	148	144	103.0	.....
	3:00 p.m.	148	144	101.8	.....
6/30/51	9:00 a.m.	160	148	102.1	Transplant soft, regular
	12:00 noon	160	142	102.0	.....
	4:00 p.m.	150	160	102.2	Penicillin administered
	11:30 p.m.	155	160	102.8	Transplant regular
7/ 1/51	10:00 a.m.	162	165	102.5	.....
	3:00 p.m.	155	160	102.5	Penicillin administered
	9:00 p.m.	160	160	102.3	Transplant fast, soft
7/ 2/51	10:00 a.m.	160	160	104.0	.....
	3:00 p.m.	165	164	104.0	Penicillin administered
	10:00 p.m.	160	158	104.0	.....
7/ 3/51	9:00 a.m.	160	150	102.4	Regular
	11:00 a.m.	160	172	102.2	Fast, regular
	3:00 p.m.	130	165	102.6	Penicillin administered; region swollen, edematous
	4:00 p.m.	128	144	102.8	.....
7/ 4/51	10:00 a.m.	140	150	104.0	Stitches removed; serum drainage
	11:00 a.m.	140	150	104.0	.....
	3:00 p.m.	120	160	103.6	Penicillin administered
	4:00 p.m.	128	160	103.2	Fast, feeble, regular
	5:00 p.m.	...	...	.....	Heart stopped; heart beat 124 hr. (5 days, 4 hr.)

Postmortem Examination

Gross: Heart appeared normal, no clots in vessels or heart cavities; adhesions from surrounding tissues to the pericardium

Pathology Laboratory Report: Degeneration, necrosis, and inflammatory cell infiltration, especially in the myocardium

freed of towels, and the bed for the heart was prepared in the subcutaneous fascia. The heart was placed in the neck so that the vessels were not twisted or compressed, and 300,000 units of crystalline penicillin was then dusted into the neck incison. The wound was then closed by interrupted sutures (Fig. 2).

On an average, the length of time that the transplanted heart was without a circulation was 40 minutes. In some instances it was as low as 30 minutes and in some as high as 45 minutes.

Except that penicillin was administered daily postoperatively, the animals required no special postoperative care. The stitches were removed on the third or fourth day (Figs. 1, 2, and 3).

RESULTS

Of 30 transplanted hearts, 23 survived and were active. The hearts that failed to manifest a controlled beat when the circulation was restored went into ventricular fibrillation almost immediately. When the weight of the pup was used as an indication of the relative size of the heart, the tendency was for the larger hearts to beat for a shorter period of time than the smaller hearts.

The transplanted hearts beat on an average of 135 times a minute. Terminally the rates became slower and irregular. In a few cases the hearts gave no indication of stopping, and a regular rhythmical beat was maintained until the end. The force of the heart usually decreased as death approached, the contractions becoming soft and less powerful. As stated, the transplanted hearts beat on an average of 129 hours, and the two hearts continued to contract for 245 and 240 hours, respectively, after removal from the pup (Fig. 3). In five of the transplants blood transfusions

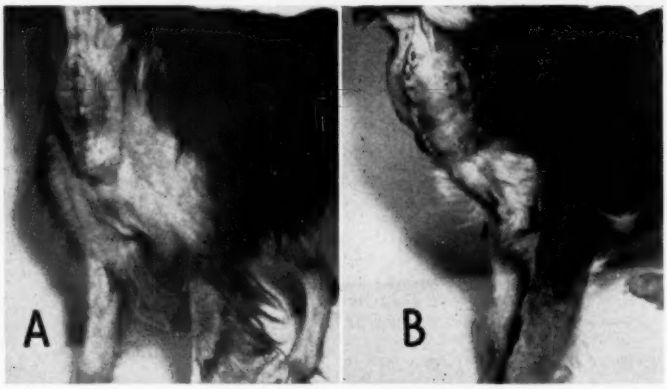

Fig. 4.—*A*, showing dog with heart transplanted into neck region. There is evidence of slight edema at base of heart. This particular heart beat for 123 hours, and photograph was taken at end of second day. *B*, showing dog with heart transplanted into neck region. There is evidence of slight edema at base of heart. This particular heart beat for 98 hours, and photograph was taken at end of third day.

were administered preoperatively from the adult to the pup hearts; these had an average survival time of 150 hours. Possibly, this is because the individuality factor was assailed by the transfusion of blood from the host to the pup, so that it became a feebler stimulus to the defensive apparatus of the recipient dog. However, we do not stress this fact, since to establish such an extremely important conclusion it would be necessary to do many more preparations, and this was not the prime function of our research (Protocol).

All sections of the transplant removed at the end of the experiment showed some cellular infiltration, varying in degree from considerable numbers of mononuclear cells, especially where there could have been some infection, to microscopic fields, which were almost devoid of these elements (Figs. 5 to 8). An occasional heart showed minimal cellular infiltration (Fig. 10). These findings indicate that the agent destroying the homotransplant was chiefly humoral and probably an antibody, rather than macrophages.

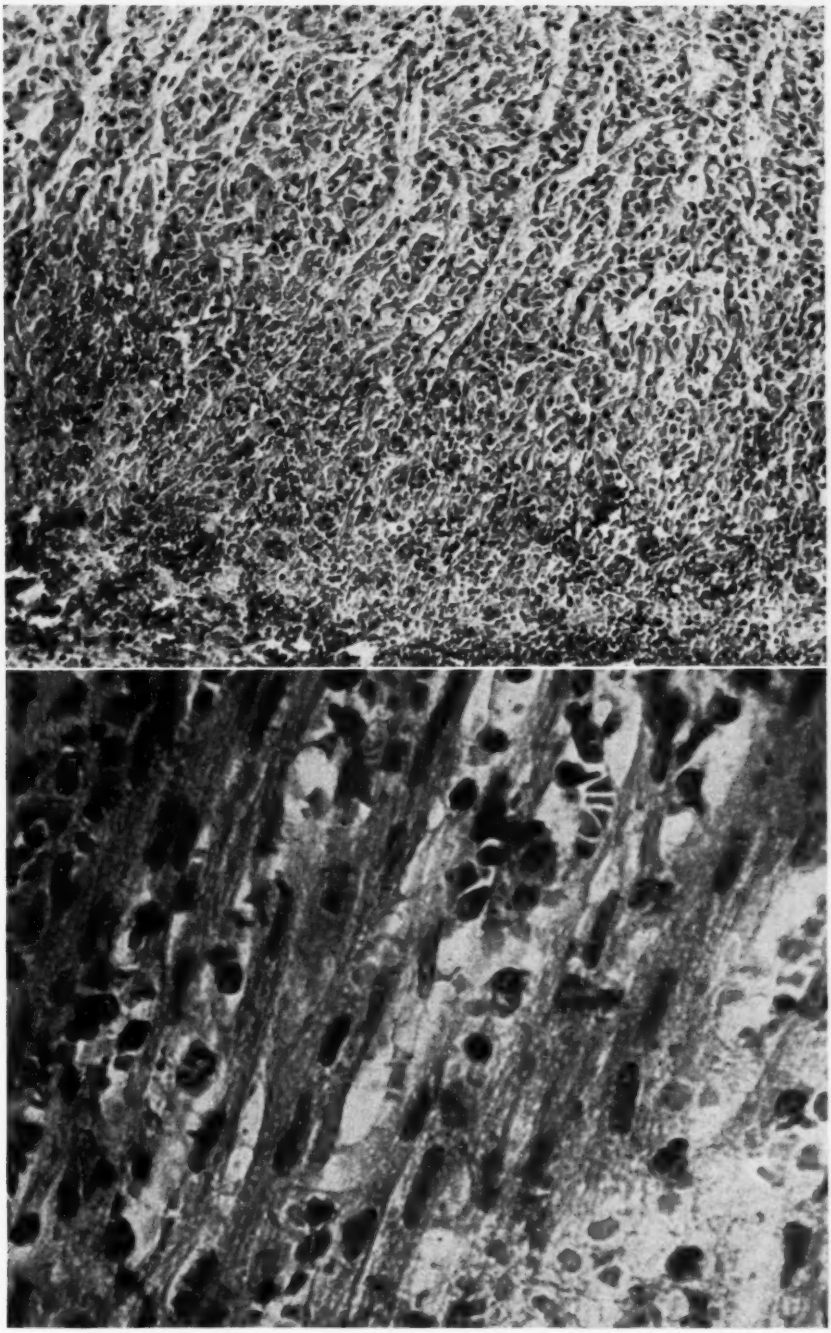

Fig. 5.—Photomicrographs, low power, × 250 (upper), and high power, × 500 (lower), of right ventricle of heart that beat for 123 hours after transplantation. Pup and adult received penicillin therapy before transplantation, and penicillin was given daily to host until transplanted heart ceased to beat.

Essential lesions in sections were areas of degeneration and necrosis, with inflammatory cell infiltration centered mainly in epicardium. There appeared to be proliferation of connective tissue, and an increased number of macrophages was noticed.

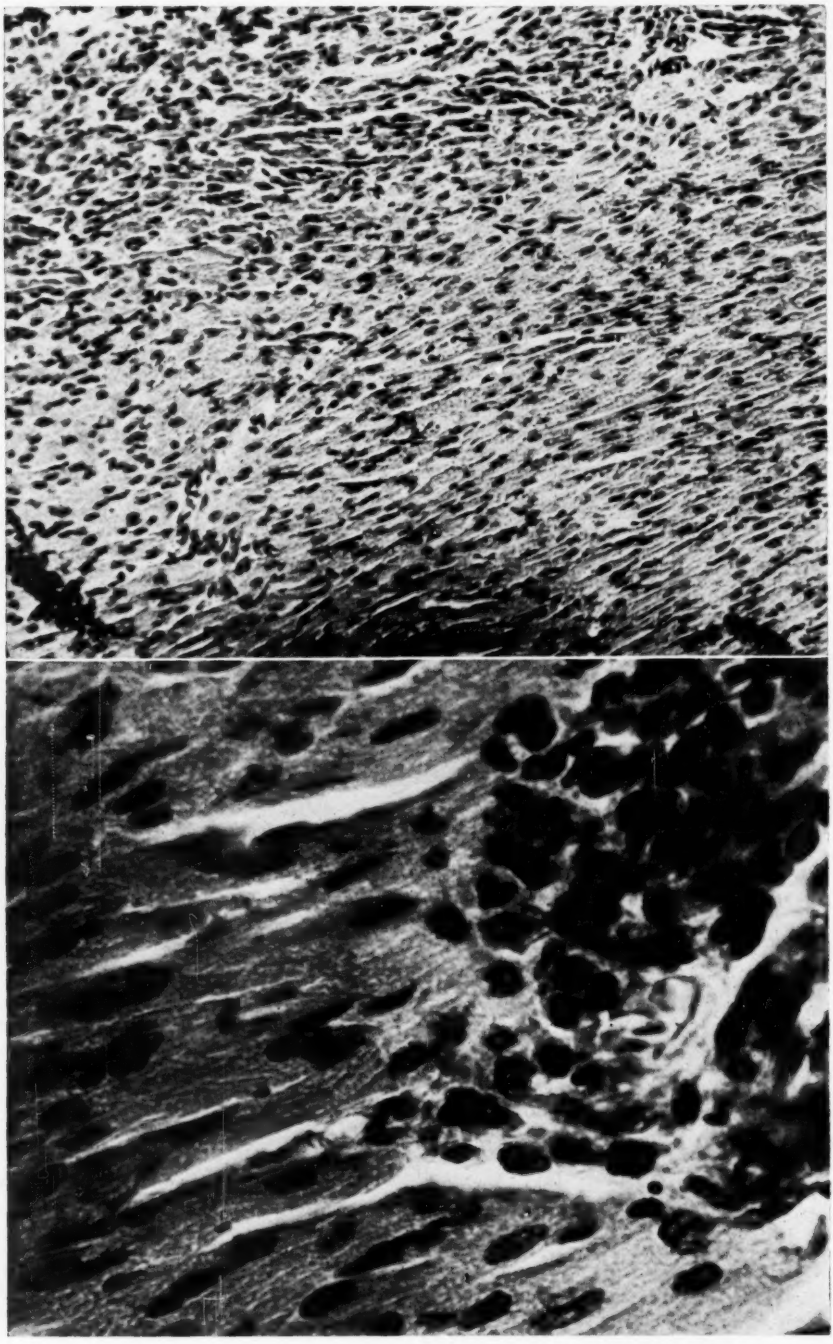

Fig. 6.—Photomicrographs, low power, × 250 (upper), and high power section, × 500 (lower), of right ventricle of heart that had beat for 124 hours after transplantation. Pup and adult host received no penicillin either before or after operation. Operation was performed aseptically.

On gross examination pericardium was greatly thickened, and myocardium of both ventricles was pale. At apex of left ventricle there were two nodules, and at this point pericardium was adherent. Nodules may have been abscesses. Microscopically there was marked proliferative pericarditis. There was myocarditis, inflammatory cells were chronic in nature, and there was beginning degeneration of muscle fibers.

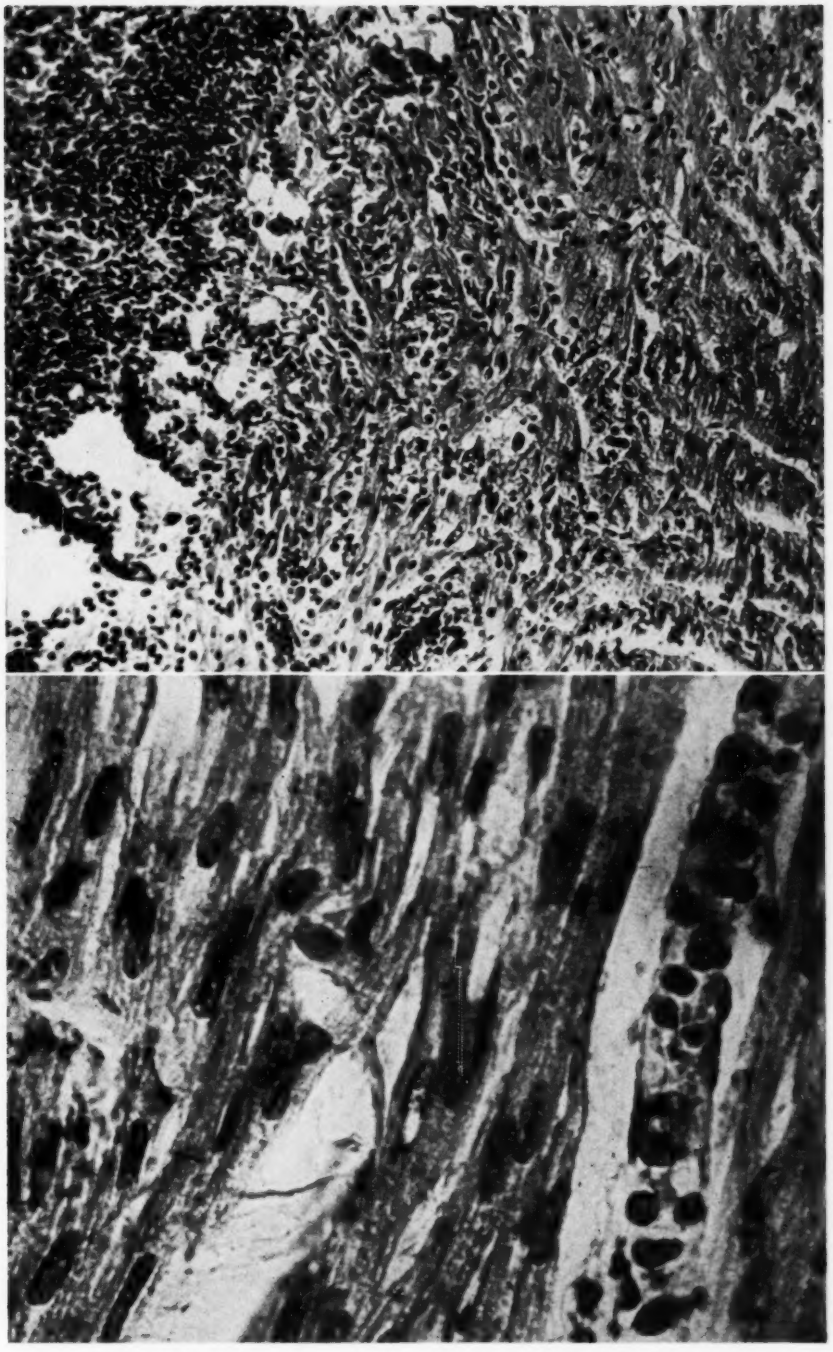

Fig. 7.—Photomicrographs, low power, × 250 (upper), and high power, × 500 (lower), of right ventricle of heart that beat for 154 hours after transplantation. Before transplantation pup received transfusions of blood from adult to which its heart was to be transplanted. Pup and host received penicillin preoperatively, and host received penicillin daily after transplantation.

There were inflammatory changes in epicardium, with rather marked changes in myocardium. There were areas of degeneration, necrosis, and inflammatory cell infiltration, with round cell, neutrophile, and fibrous tissue proliferation. Left ventricle showed some inflammatory cell infiltration between muscle fibers, but the muscle fibers themselves appeared essentially normal.

Fig. 8.—Photomicrographs, low power, × 250 (upper), and high power, × 500 (lower), of right ventricle of heart that beat for 240 hours after transplantation. Pup and adult host received penicillin preoperatively, and host received penicillin daily after transplantation.

There was fibrinous pericarditis with infiltration of lymphocytes and neutrophiles. Myocardium was diffusely affected. Muscle fibers in some areas were widely separated with an exudate containing both lymphocytes and neutrophiles. In other areas muscle fibers had undergone degeneration and necrosis.

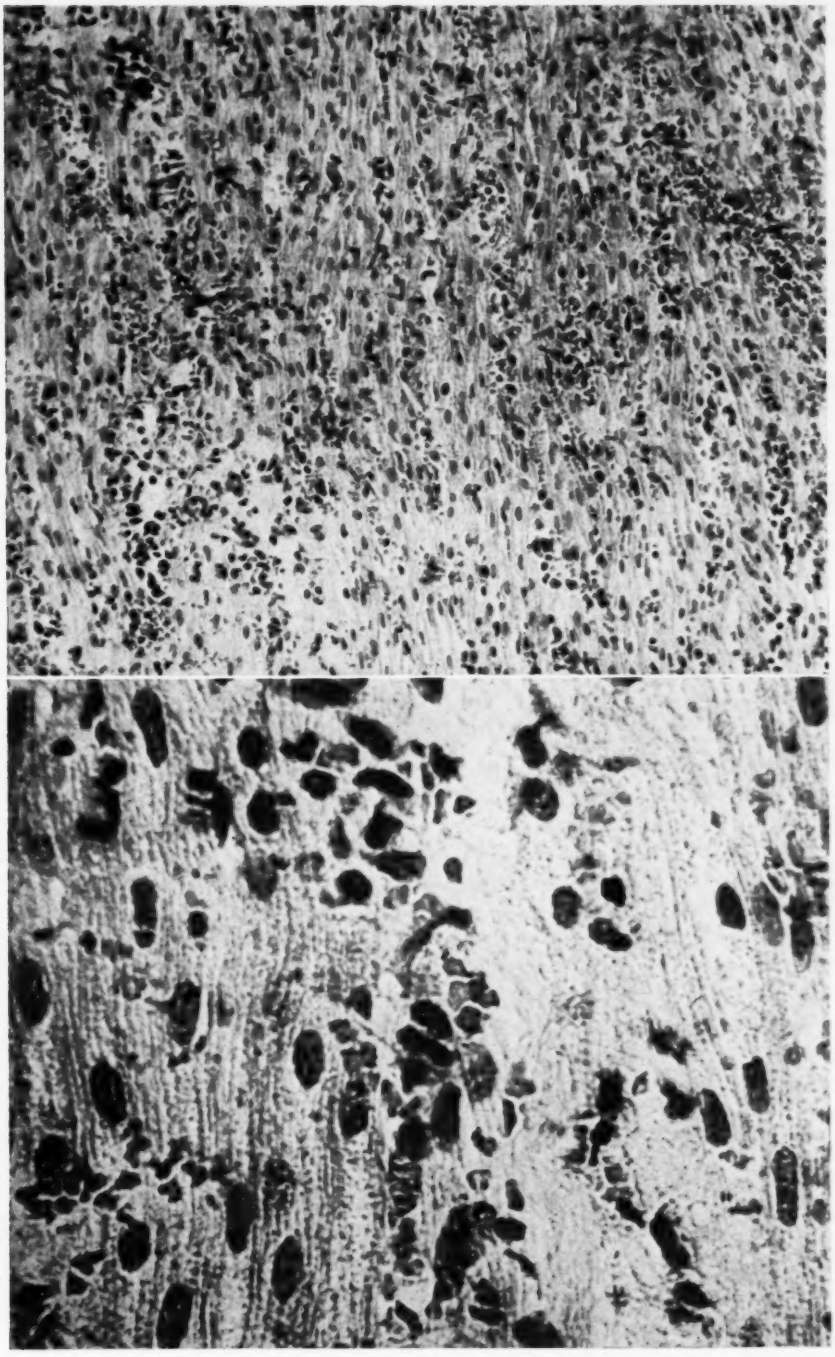

Fig. 9.—Photomicrographs, low power, × 250 (upper), and high power, × 500 (lower), of right ventricle of heart that beat for 245 hours after transplantation. Before transplantation pup received transfusions from adult to which its heart was to be transplanted. Host received penicillin daily after transplantation.

Lesions were chiefly those of slight cell infiltration, nature of which was both mononuclear and neutrophilic. Nuclei of muscles appeared healthy. Longitudinal and cross striations in muscle fibers are still rather apparent.

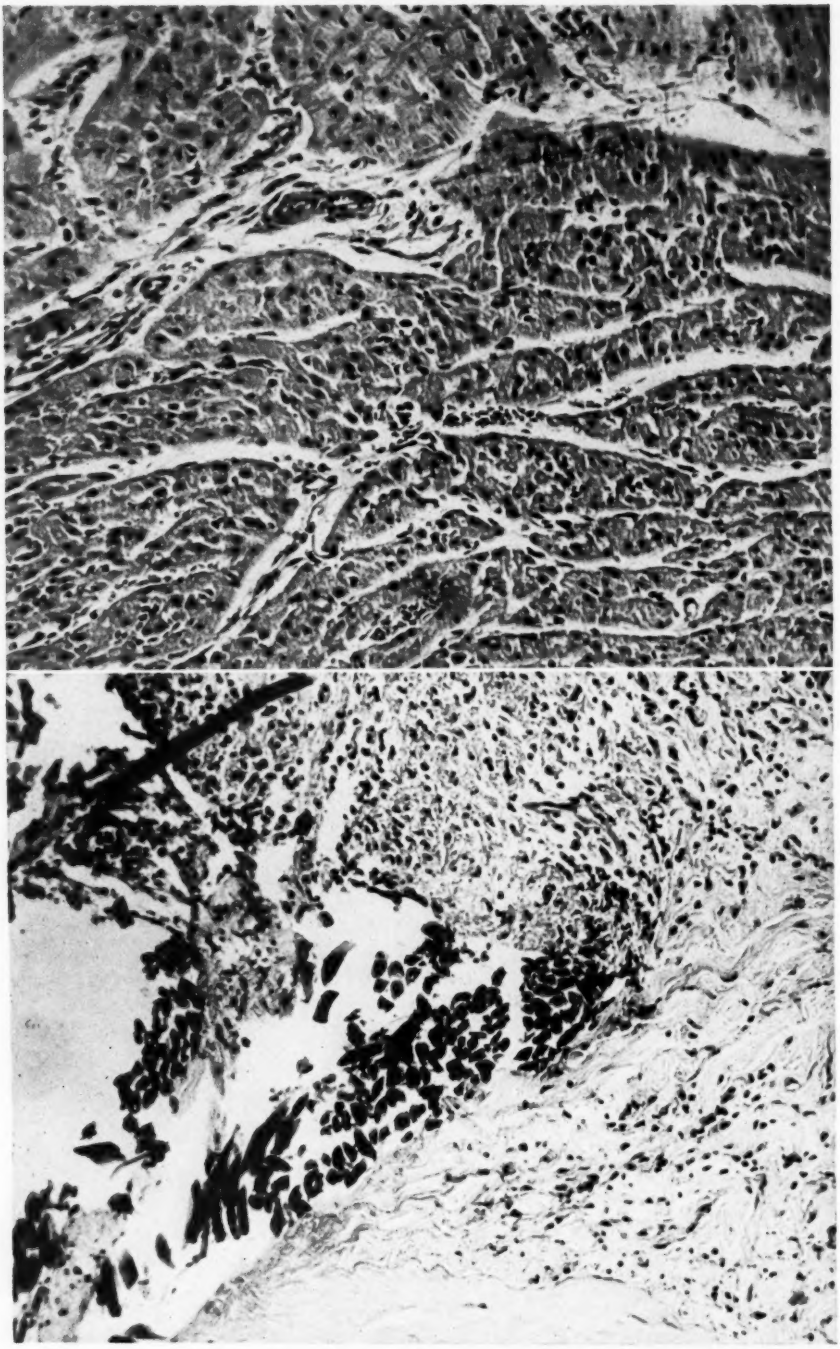

Fig. 10.—Upper, photomicrograph, low power, × 250, at point of anastomosis of subclavian artery to carotid artery of host. Vessels were united, and heart beat for 245 hours.

Anastomosis was intact, and silk fibers from suture material did not appear to be producing extensive cellular reaction. Surrounding tissues showed areas of degeneration and necrosis, with increase in number of connective tissue cells.

Lower, photomicrograph, low power, × 250, of right ventricle of transplanted heart that beat for 96 hours. Section showed degeneration and necrosis of muscle fibers in some areas, with minimal inflammatory cell infiltration of both neutrophiles and lymphocytes.

COMMENT

It should be emphasized that this is a coronary viviperfusion, purely (Fig. 1). Blood from the carotid artery finds its way to the aorta of the transplanted heart and forces the semilunar valves to close. The blood tracks through the coronary system and is ejected from the right ventricle via the pulmonary artery into the blood stream of the host. The prime factor in resuscitating the quiescent transplant is an adequate intracoronary pressure.

Assuming the coronary circulation to be about one-sixth the total circulation, and bearing in mind that the right heart in this preparation is operating against a pulmonary arterial pressure of about 2 mm. Hg (since there is no peripheral resistance), it can be seen that the work of the transplanted heart is small indeed, possibly of the order of 1 or 2% of that of the normal heart. It may be regarded as doing no work in the usual physical sense, although a considerable volume of blood is expelled from its chambers. It is possible, though not probable, that the resuscitation of a heart from which one expects the usual amount of work would not be so simple; however, the resuscitation of a dead dog by means of an intra-arterial transfusion containing epinephrine is evidence that even when a heart is called upon to do work it can be resuscitated by the simple means of raising the intracoronary pressure to a suitable level (Crile [2]).

Mann and his associates [3] (1933) performed a series of transplants with the intact heart of a pup. They stated that the pulsation of the transplant was resumed promptly, three times out of four. The average rate of pulsation was 100 to 130 beats a minute, and the rate was almost constant. The average survival time was four days; they had one heart that survived for eight days. They state that on postmortem examination ecchymosis was present on the surface of the heart, and on section the muscle tissue was friable. Extensive edema was present around many of the hearts in the neck region of the adult. Microscopic sections of the heart showed that many areas were completely infiltrated with lymphocytes, large mononuclear cells, and polymorphonuclear lymphocytes. Few normal muscle fibers were present.

Our technique is an elaboration of theirs, and our results differ in some respects. In the first place, our heart had a longer survival period. This we attribute to two factors: (1) the use of penicillin, which definitely inhibited infection both from the blood stream (if any) and from the operative site, and (2) the use of blood vessel suture material, which can be purchased in convenient form today from commercial houses. We feel that this material is better than that which Mann and his associates had available.

The big difference between our results and theirs is in the histological appearance of the transplanted heart tissue at the termination of the experiment. In many cases, sections from our hearts showed almost no leucocytic infiltration. Thus, it is evident that the ultimate failure of the homotransplant to function indefinitely depends more on humoral agencies than on attack by the cellular defenses of the host (Figs. 5 to 10).

2. Crile, G. W.: Anemia and Resuscitation: An Experimental and Clinical Research, New York, Appleton-Century-Crofts, Inc., 1914.

3. Mann, F. C.; Priestley, J. T.; Markowitz, J., and Yater, W. M.: Transplantation of the Intact Mammalian Heart, Arch. Surg. **26**:219, 1933.

Marcus, Wong, and Luisada,[4] 1951, reported on a method for the transplantation of the heart in dogs. They maintained an uninterrupted blood supply to the coronary arteries of the heart during the entire operation, involving the use of a third animal. An intra-atrial septal defect was made as a precaution against dilation of the right heart in some cases.[3] Although they state that the transplantation of the heart was successful in 10 experiments, none of the hearts beat for longer than 48 hours, a figure greatly surpassed in our experiments and in those by Mann and his associates, in which the average survival time was four days.

In the present state of knowledge it is not likely that homotransplantation of the usual tissues afflicted by disease will achieve great prominence clinically. With the exception of blood transfusion and transplantation of the cornea, homotransplantation of tissues has a melancholy record of failure in surgery. In extensive burns, homotransplantation of skin may have the emergency function of combating loss of plasma through the denuded areas, so that the patient may be tided over his shock, but the consensus is that such transplants have only a limited survival. The attempt to transplant tissues successfully from one subject to another is probably lacking in certain fundamental pieces of knowledge, much as is the case with our knowledge of carcinogenesis. In the one case we do not know why a cell continues to proliferate when it should not. In our case we do not know why a cell invites destruction when it ought to survive.

SUMMARY

A series of 23 homotransplantations of the dog heart was done, the heart of a pup being anastomosed to the vessels of the neck of an adult dog. Such a preparation is really a viviperfusion and does no work, although it pulsated regularly for an average of 129 hours. The ultimate failure of such a transplant depends on the usual biological reaction to a homotransplant. Some of the sections of the transplanted heart removed at the termination of the experiment showed remarkably little cellular infiltration, suggesting that a humoral agency was responsible for the destruction of the transplant.

The interest and helpful criticism of Dr. J. Markowitz, of the Department of Physiology, University of Toronto, are acknowledged.

Dr. Schroder, of the Department of Pathology, Ontario Veterinary College, prepared the microscopic sections.

Dr. H. Neely, of the Department of Anatomy, Ontario Veterinary College, made the photomicrographs, and Dr. J. Archibald, Department of Medicine, cared for the animals.

4. Marcus, E.; Wong, S. N. T., and Luisada, A. A.: Homologous Heart Grafts: Transplantation of the Heart in Dogs, Surgical Forum: Proceedings of the Forum Sessions, Thirty-Seventh Clinical Congress of the American College of Surgeons, San Francisco, Nov., 1951, Philadelphia, W. B. Saunders Company, 1952, p. 212.

ABDOMINOPERINEAL OPERATION FOR HIGH IMPERFORATE ANUS IN THE NEWBORN

HARVEY R. BUTCHER, M.D.
ST. LOUIS

UNTIL recently, an infant born with an imperforate anus and a high rectal pouch, as revealed by x-rays or perineal exploration, was subjected to a colostomy and the repair of the anomaly deferred until later. In 1948 J. E. Rhoads [1] described two cases in which colostomy was not done but instead an abdominoperineal procedure carried out shortly after birth as the complete and final operation. The present report deals with six newborn infants in whom a similar procedure was carried out without operative mortality.

PREVIOUS WORK

Of the two cases reported by Rhoads, in one the result was completely successful and in the other the infant died four months after surgery of renal failure due to hydronephrosis but with a normal functioning gastrointestinal tract. Shortly after this report, Norris [2] discussed four cases in which treatment was similar, with successful results in two, failures being due to associated anomalies. Santulli,[3] in reporting a series of cases of imperforate anus, described seven newborn who were treated by primary abdominoperineal replacement, with no mortality. The operative technique was well illustrated, but no clinical details were presented. Moore and Lawrence [4] performed abdominoperineal anorectoplasty as the primary procedure at birth in seven cases, the details of which were not given. However, in discussion on Moore and Lawrence's paper, Robert Gross and C. Everett Koop mentioned much larger numbers of cases in which this procedure was performed, but no details of their experiences were mentioned.

PRESENT DATA

At the St. Louis Children's Hospital during the past three years, six infants with imperforate anus have been treated at birth by primary abdominoperineal

From the Department of Surgery, Washington University School of Medicine, and St. Louis Children's Hospital.

1. Rhoads, J. E.; Pipes, R. L., and Randall, J. P.: A Simultaneous Abdominal and Perineal Approach in Operations for Imperforate Anus with Atresia of the Rectum and Rectosigmoid, Ann. Surg. **127**:552, 1948.

2. Norris, W. J.; Brophy, T. W., III, and Brayton, D.: Imperforate Anus: A Case Series and Preliminary Report on the One Stage Abdominoperineal Operation, Surg., Gynec. & Obst. **88**:623, 1949.

3. Santulli, T. V.: The Treatment of Imperforate Anus and Associated Fistulas, Surg., Gynec. & Obst. **95**:601, 1952.

4. Moore, T. C., and Lawrence, E. A.: Congenital Malformations of the Rectum and Anus: Clinical Features and Surgical Management in 120 Cases, Surgery **32**:352, 1952.

anorectoplasty. All fall into the Class III category described by Ladd and Gross.[5] Patients having this operation as a secondary procedure following previous colostomy are not included. These cases are briefly described as follows.

CASE 1.—A white infant boy (weight 2,268 gm.) was born on Dec. 21, 1951, after a normal pregnancy and delivery. An imperforate anus was noted at birth. On admission to the St. Louis Children's Hospital, other congenital anomalies were noted consisting of right anophthalmos, with a coloboma of the iris choroid and retina, and a bifid scrotum and hypospadias, although both testes were descended. The patient passed some urine and meconium per urethra. In the region of the anus only a small dimple was present. Thirty-six hours after birth a primary abdominoperineal operation was carried out. The rectum was high and terminated as a fistulous tract which entered the posterior urethra. After adequate mobilization, the fistula was divided and the distal end tied. The rectum was pulled through and sutured to the skin through a perineal incision at the anal dimple. No blood supply to the distal rectum had to be sacrificed to obtain adequate length of rectum with which to insure suture to the perineal skin without tension. The postoperative course was complicated by the development of diarrhea and feeding problems. However, the patient was finally discharged in fair condition. Since that time the child's nutritional status has improved, and, when last seen 10 months later, he was having normal stools and continuing to gain weight.

CASE 2.—A white infant boy was born on Feb. 14, 1952, after a normal pregnancy and delivery. The absence of an anus was noted at birth, and the patient was immediately transferred to the St. Louis Children's Hospital where examination revealed slight abdominal distention and no anal opening. His weight was 3,270 gm. X-rays taken with the patient inverted (Wangensteen and Rice technique[6]) revealed the pocket of air to be 2.5 cm. from the skin. Seven hours after birth a combined abdominoperineal operation was carried out after complete mobilization of the rectum, a small fistula between the distal rectum and the prostatic urethra being tied and cut. The mobilized rectum was then brought through the perineum in the region of the anal dimple, where an opening was developed by means of gentle blunt dissection and the excision of a small circle of skin. The fibers of the anal sphincter were identified on each side of the perineal opening. The rectal mucosa was then sutured to the skin without tension. No blood supply to the distal rectal stump had to be sacrificed. The patient's postoperative course was entirely uneventful except for the development of intestinal obstruction on the 10th day. This was relieved by laparotomy and division of a band. After this, a superficial wound infection developed which healed rapidly. At the time of discharge it was possible to insert the little finger with ease into the rectum, gentle dilations having been carried out during the postoperative period. When last seen, seven months after operation, the patient appeared to be normal as far as weight and nutrition were concerned, and the anal aperture was quite adequate. Slight mucosal redundancy was present, for which surgical correction may be considered at a later date.

CASE 3.—A white infant boy was born on July 20, 1952, after normal pregnancy and delivery at home. An imperforate anus was noted 12 hours after birth because of the absence of stools. On admission physical examination revealed the imperforate anus and slight abdominal distention, but no abdominal tenderness. Both testes were undescended; otherwise, the infant appeared normal. Urine was voided per urethra and showed only a few epithelial cells. X-rays revealed the rectal pouch to be approximately 5 cm. from the skin marker. A primary abdominoperineal operation was carried out. A high rectum was found ending in a fistulous cord which was attached in the region of the posterior urethra. The cord was ligated. In order to suture the rectum to the skin without tension, it was necessary to sacrifice the superior hemorrhoidal vessels. This was done some distance from the bowel wall and without evident impairment of blood supply. The patient's postoperative course was complicated by partial wound separation on the third postoperative day. After closure of this, however, the course was uneventful. At the time of discharge, the patient was having stools normally and was without evidence of stricture.

5. Ladd, W. E., and Gross, R. E.: Abdominal Surgery of Infancy and Childhood, Philadelphia, W. B. Saunders Company, 1941.

6. Wangensteen, O. H., and Rice, C. O.: Imperforate Anus: A Method of Determining the Surgical Approach, Ann. Surg. **92**:77, 1930.

He was last seen four months later and appeared to be a normal healthy infant, eating well and averaging two stools per day. Sphincter action was thought to be present, and the anus admitted the entire fifth finger with ease. Two transient episodes of difficulty in voiding had occurred which cleared spontaneously. Subsequent intravenous pyelograms have revealed left hydronephrosis, with bifid left renal pelvis and double left ureter.

CASE 4.—A white infant boy entered the hospital 46 hours after birth, having been delivered at home without incident. His weight was 4,070 gm. The pregnancy and delivery were apparently normal. On examination after admission, findings revealed a mongoloid infant with evidence of congenital heart disease. Also present was an undescended left testicle and marked abdominal distention. X-rays revealed rectal air 3 cm. from the perineal skin. The parents insisted on operation despite the full knowledge of the mongoloid state of the infant. On March 5, 1950, a primary abdominoperineal operation was carried out. A hugely distended blind distal colon, thought probably to be of the "Hirschsprung type," was found. This was resected along with a fibrous cord attached to the base of the bladder. The proximal normal colon was then brought to the anal skin after dividing one of the major mesenteric vessels. Postoperatively the patient had normal stools and voided without difficulty. However, he gradually deteriorated, with more and more frequent episodes of cyanosis developing. Death occurred 18 weeks later and was felt to be related to the congenital heart condition. Postmortem examination revealed a ventricular septal defect, dextraposition of the aorta, and transposition of the great vessels.

CASE 5.—A white infant, born on July 18, 1951, was admitted to St. Louis Children's Hospital 24 hours after a normal full-term delivery. Examination revealed an imperforate anus, a rectovaginal fistula, and congenital heart disease which to date is incompletely diagnosed. It was not possible on physical examination to determine the sex of the infant. Meconium and urine were seen to exude from a perineal opening which was thought to be, by various observers, either urethral or vaginal. On July 25, a primary abdominoperineal operation was carried out, the blind high rectum ending in what was considered a vaginal fistula which was ligated and cut. A bicornate uterus and two ovaries were identified. Blood supply to the distal rectum had to be partially sacrificed to obtain adequate length, after which the rectum was sutured without tension to the perineal skin. During the postoperative course, difficulty in voiding occurred requiring an inlying catheter for several days. This eventually corrected itself, although after discharge the patient had one episode of urinary infection and distention of the bladder which responded to furtrethonium iodine administration. When last seen 15 months later, the patient was having no further difficulty, stools passing normally and there being no evidence of stricture.

CASE 6.—After normal pregnancy and delivery, this white infant boy was noted to have imperforate anus and was admitted 24 hours after birth. His weight was 3,700 gm. On physical examination the patient was noted to have typical mongoloid characteristics without other gross abnormalities except for the imperforate anus. The genitalia were normal. After full discussion with the parents of the mongoloid nature of the infant, a primary abdominoperineal operation was carried out. No blood supply had to be sacrificed and the distal rectum was brought through a perineal opening which was thought to be surrounded by sphincter and sutured to the skin without tension. The postoperative course was entirely uneventful, the rectal dilation being started approximately 10 days after operation. One and one-half years later, the patient's rectal opening appeared adequate, and he was slowly gaining weight, although his mongoloid characteristics were still very apparent and his mental deficiency evident. Weekly anal dilations by the mother were still being performed.

COMMENT

The six cases without operative mortality described herein illustrate the feasibility of primary abdominoperineal anorectoplasty in newborn infants with imperforate anus and a rectal pouch too high to be approached through the perineum. This procedure has several advantages over previous plans of treatment. These are principally (1) avoidance of colostomy and subsequent operations; (2) success-

ful repair of rectourinary fistulae in males, thus averting episodes of renal infection, and repair of rectovaginal fistula in females, and (3) the early determination of the sex of the infant when this is not possible by external examination.

Certain technical factors in performance of primary abdominoperineal anorectoplasty warrant emphasis.

1. Careful perineal dissection and identification of the anal sphincter is indicated. In this manner the center of the sphincter may be identified and approached by gentle blunt dissection, both from above with a finger along the curve of the sacrum and coccyx, and from below through the areolar tissue occupying this area.

2. Gentle dilation of the external sphincter to adequate size is important, although stenosis is still a problem.

3. An important factor in averting late stenosis is adequate length of rectum with good blood supply at its distal end sutured to anal skin without tension so that primary union results. To obtain adequate length, it is occasionally necessary to sacrifice the superior hemorrhoidal vessels. This has not resulted in sufficient impairment of blood supply to require resection of the most distal portion of the rectum in the two cases in which it was carried out. However, in some cases, segments of the distal rectum may have to be resected, but the length gained will more than suffice for that lost. In one case in the present series, because of intrinsic disease, part of the distal rectum was resected without interfering with the formation of a good anastomosis without tension.

Late results of this operation for imperforate anus in infants will depend in part on associated congenital anomalies. This has been stressed by others. In the present small series, these consisted primarily of mongoloidism, congenital heart disease and various types of genitourinary anomalies. The need for obtaining complete data on the urinary tract should be emphasized because of the high evidence of genitourinary anomalies. In all cases, palpation of kidneys at time of operation should be carried out. Routine pyelographic studies should also be performed. Of special interest was bladder atony, which occurred in Case 5 and seemed similar to that seen frequently in adults after abdominoperineal resection of the rectum. Whether this was due to nerve injury at the time of operation or to congenital defect itself is not certain.

SUMMARY

Six infants with imperforate anus and high rectal pouch were subjected soon after birth to primary abdominoperineal anorectoplasty with no operative mortality. This experience, including certain technical features of the procedure, is described. Despite the many advantages of the operation, an important and discouraging prognostic aspect is the frequency of other serious and irremediable congenital anomalies.

POSTMASTECTOMY EDEMA OF THE ARM

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EDEMA of the arm following radical mastectomy for carcinoma of the breast, in the absence of metastatic or recurrent disease in the axilla, has a reported incidence of from 10 to 50%. The edema varies in severity from a mild almost unnoticeable enlargement to massive swelling; disability may be so pronounced as to preclude use of the arm even to perform simple household tasks. There are many methods advocated for prevention and treatment of the condition, but the exact cause of the edema remains in doubt.

HISTORICAL

Halsted,[1] in 1921, published the first article dealing with elephantiasis chirurgica. It was his opinion that blockage of the lymphatic and venous channels predisposed toward edema but that it was necessary for infection to occur before the edema became significant. In particular, he believed that primary closure, with tenting of the skin across both axillary and infraclavicular spaces, which permitted pooling of blood and serum, encouraged infection and subsequently edema. Adoption of the skin-grafting closure, with meticulous attention to suturing down the skin in all depressions, greatly lowered the incidence of swollen arms seen at the Johns Hopkins Hospital. Reichert,[2] working with Halsted, showed that in dogs the thigh could be severed, except for the artery, vein, nerve, and bone, and then resutured without the occurrence of significant edema postoperatively. Lymphatic vessels bridging the scar could be demonstrated by the end of the fourth day. However, if the scar was widened, as with infection, new lymphatic vessel formation was greatly delayed, if not completely prevented.

Peck and White,[3] in 1922, reported that they found retention of the pectoralis minor muscle advisable "either by division and resuture, or better, by retraction for axillary dissection," in that it protected the axillary vessels from contracting cicatrices and minimized the danger of postoperative edema. They subsequently abandoned the procedure because of adverse criticism, based on the premise that

From the Department of Surgery, Bowman Gray School of Medicine of Wake Forest College, Winston-Salem.

1. Halsted, W. S.: Swelling of the Arm After Operations for Cancer of the Breast: Elephantiasis Chirurgica, Its Cause and Prevention, Bull. Johns Hopkins Hosp. **32**:309-313, 1921.

2. Reichert, F. L.: Regeneration of the Lymphatics, Arch. Surg. **13**:871-881, 1926.

3. Peck, C. H., and White, W. C.: Tumors of the Breast, Ann. Surg. **75**:641-651, 1922.

they were not doing a complete radical mastectomy. (Gray,[4] in 1935, demonstrated that the breast lymphatics do not permeate the fascial sheath of the pectoralis minor, but sweep around the lateral edge of the muscle. Thus, division and resuture of the muscle, unless the muscle is directly invaded by the tumor, would seem to preserve the principle of radical mastectomy.)

Veal, in 1937,[5] and again in 1938,[6] stated that occlusion of the axillary vein played a significant part in causing edema of the arm. He classified the edema into (1) pure lymphatic obstruction, which accounted for about 10% of the cases; (2) venous occlusion, due to constriction of the axillary vein, either intermittent or complete, which accounted for about 90% of cases, and (3) a combination of 1 and 2 called combined lymphatic and venous obstruction. This was said to be rare, and its incidence was not given. Roentgen visualization of the axillary vein and collaterals with thorium dioxide (Thorotrast) was performed in 46 cases of persistent edema. In 90% of the cases some encroachment of the lumen of the vein was seen. Veal suggested that placing fat over the axillary vessels would protect the vessels from constrictive scarring and might lower the incidence of edema.

Holman, McSwain, and Beal [7] in an analysis of 100 cases found that infection and roentgen-ray dermatitis were the two factors most often associated with massive edema. In contradistinction to Halsted's earlier work, they found that skin grafting did not play an appreciable part in the causation of edema. Also, they noted that preoperative metastases to the axillary nodes did not influence the appearance of edema.

MacDonald [8] found that resection of the axillary vein enabled him to perform a more thorough dissection of the axilla and also seemed to lower the incidence of postoperative edema. He believed "the sequel of events leading to postmastectomy lymphedema are fat necrosis in the operative field, secondary infection, regional (perivenous) axillary lymphangitis with sclerosis, and obstruction. Obesity is the most important single predisposing factor in the genesis of lymphedema." (Veal [9] had reported previously that complete occlusion of the vein, as demonstrated by venography, stimulated the formation of collateral veins. This may explain MacDonald's success with ligation of the vein.)

Hollenbach [10] reported that he prevented edema in 330 cases by transferring the insertion of the pectoralis minor muscle laterally to surround completely the stripped vein and artery with muscle. He dissected the insertion free and elevated the muscle, so that an adequate axillary dissection could be performed, and then

4. Gray, J. H.: Interim Report of an Investigation of the Lymphatic System, St. Barth. Hosp. Rep. **69**:322-324, 1936.

5. Veal, J. R.: Swelling of the Arm Following Radical Mammectomy: Role of Axillary Vein in Production of Edema of Arm Following Radical Removal of Breast, J. A. M. A. **108**:1236-1241, 1937.

6. Veal, J. R.: Pathologic Basis for Swelling of the Arm Following Radical Mastectomy, Surg., Gynec. & Obst. **67**:752-760, 1938.

7. Holman, C.; McSwain, B., and Beal, J. M.: Swelling of the Upper Extremity Following Radical Mastectomy, Surgery **15**:757-765, 1944.

8. MacDonald, I.: Resection of the Axillary Vein in Radical Mastectomy: Its Relation to the Mechanism of Lymphedema, Cancer **1**:618-624, 1948.

9. Veal.[5,6]

10. Hollenbach, F.: Vermeidung des Armödems nach Mamma-Amputation, Chirurg **20**:374-375, 1949.

used the muscle as a pedicle graft. He attributed his success to the prevention of cicatrization around the axillary vein. Hollenbach was of the opinion that lymph stasis was of little or no importance and cited Dietrich to the effect that lymph is reabsorbed adequately by the blood vessels when the circulation is adequate.

Daland [11] analyzed the postmastectomy cases encountered at the Pondville Hospital and found that 6.5% of the patients had severe edema and 17% had moderate swelling. He attributed this "low incidence" to prevention of sepsis, not allowing the incision to extend onto the arm, drainage of the wound, use of x-ray therapy for adequate reason only (not prophylactically), and early motion of the arm. Guthrie and Clough [12] attributed their low incidence of postoperative edema (6% moderate, 2% severe) to a technique which included (1) keeping the incision off the arm, (2) sharp anatomic dissection of the axillary space, which protects it against infection, (3) not using drains, and (4) wide mobilization of the arm early. Curiously, these two reports are nearly similar, except for the use of drains, yet Daland's incidence of edema was three times that of Guthrie's.

Parker [13] believes that the edema is due to thrombosis of the axillary vein and if early edema is prevented by elastic bandaging of the arm recanalization occurs. He keeps the potentially affected arm bound for eight weeks and reports that no edema occurred in the 48 patients who had this treatment. In two patients on whom the rubberized bandage was allowed to remain only four to five weeks, there was a 100% incidence of edema.

The above summary represents some of the viewpoints concerning the causes and prevention of postmastectomy edema. In an effort to properly assess the part various factors might play in causation of the edema, 24 postradical mastectomy patients were studied in regard to venous pressure, arterial pressure, arm measurements, use of arm, type of carcinoma, extent of carcinoma, postoperative infection, grafting, and use of x-ray therapy, the side not operated on being used as a control.

METHODS

Consecutive patients free of recurrence after radical mastectomy, seen in the Tumor Clinic of the North Carolina Baptist Hospital, were studied at postoperative intervals which varied from one week to seven years. The arterial pressure in each arm was determined with a sphygmomanometer. Venous pressure was taken directly from the antecubital vein, using isotonic sodium chloride solution as the indicating fluid; measurements were repeated on each side until two or more readings agreed within 1 cm. Arm circumferential measurements were taken at the largest points on the arm and forearm and at the wrist. The use of the arm was classified by the following arbitrary scale:

Excellent	Normal activity
Very good	Able to put hand to nape of neck easily
Good	Uses hand for housework but tires easily
Poor	Can hold objects but at waist level only
Incapacitated	Uses fingers only

The type of carcinoma, extent of the carcinoma, postoperative infection, grafting, and use of x-ray therapy were ascertained from the patient's chart in each case.

11. Daland, E. M.: Incidence of Swollen Arms After Radical Mastectomy and Suggestions for Prevention, New England J. Med. **242**:497-502, 1950.

12. Guthrie, D., and Clough, D. M.: Carcinoma of the Breast, Pennsylvania M. J. **53**:497-500, 1950.

13. Parker, J. M.: Prevention of Lymphedema of the Upper Extremity After Radical Mastectomy: Preliminary Report, Am. Surgeon **17**:849-852, 1951.

RESULTS

Of the 24 patients, 12 exhibited some degree of edema (some part of the affected arm measured at least 2 cm. larger in circumference than the corresponding part of the contralateral arm). Only two showed edema of 6 cm. or more (Cases 2 and 11, Table). Eight of the patients showed a difference of 10 mm. or more

Summary of Data

Case	Type Carcinoma	Axillary Metastasis	Graft	Infection	X-Ray Therapy	Use of Arm	Postoperative, Mo.	Mensurations					
								Side*	Midarm, Cm.	Forearm, Cm.	Wrist, Cm.	Venous Pressure, Mm. Saline	Arterial Pressure, Mm. Hg
1	Mixed	No	No	No	No	Exc.	16	A	26	25	16	247	148/78
								B	25	24	16	240	150/80
2	Scirrhous	No	No	No	Yes	Exc.	66	A	38	34	24	190	210/110
								B	25	22	15	185	220/118
3	Scirrhous	No	No	No	Yes	Exc.	80	A	27	26	17	120	136/80
								B	26	24	15	170	150/80
4	Intraductal	Yes	No	Yes	Yes	Exc.	75	A	29	24	16	154	128/88
								B	27	24	16	160	130/90
5	Scirrhous	Yes	No	No	Yes	Exc.	25	A	18	18	14	72	100/66
								B	18	18	14	67	98/66
6	Scirrhous	No	No	No	Yes	Exc.	54	A	28	26	16	182	118/80
								B	27	25	16	138	130/88
7	Scirrhous	No	No	Yes	Yes	Exc.	51	A	27	23	16	110	136/90
								B	25	23	15	120	140/90
8	Mucoid	No	No	No	Yes	Exc.	38	A	25	23	15	160	112/80
								B	24	23	15	170	114/80
9	Scirrhous	Yes	No	No	Yes	Good	44	A	29	25	16	218	120/78
								B	30	25	16	221	120/78
10	Scirrhous	No	No	No	No	Exc.	36	A	20	19	15	120	122/74
								B	21	19	15	122	124/72
11	Medullary	Yes	Yes	Yes	Yes	Good	18	A	31	24	16	151	140/90
								B	25	24	16	148	150/90
12	Scirrhous	Yes	No	No	No	Good	12	A	30	27	18	190	210/120
								B	29	25	16	210	212/130
13	Mucoid	Yes	No	No	No	Poor	1/4	A	26	24	16	170	110/70
								B	25	23	15	175	100/74
14	Duct cell	Yes	No	Yes	Yes	Good	21	A	30	24	16	263	175/110
								B	28	23	15	265	195/110
15	Comedo	No	No	No	No	Exc.	19	A	27	25	16	240	110/70
								B	25	23	15	150	110/70
16	Scirrhous	No	Yes	No	No	Exc.	17	A	22	21	15	206	140/96
								B	22	20	14	180	142/78
17	Scirrhous	No	No	No	No	Exc.	9	A	33	26	17	220	150/90
								B	32	26	17	220	150/80
18	Scirrhous	No	No	No	No	Exc.	9	A	25	25	15	125	112/70
								B	23	23	15	120	112/70
19	Scirrhous	No	No	No	No	Exc.	6	A	27	22	14	160	180/90
								B	25	22	14	140	170/80
20	Duct cell	Yes	Yes	No	No	Very good	2	A	19	20	14	150	112/70
								B	19	18	13	160	108/70
21	Duct cell	No	No	No	No	Good	1/4	A	27	24	15	140	108/70
								B	24	23	15	223	110/74
22	Duct cell	No	No	No	No	Good	1/4	A	24	22	13	110	110/70
								B	22	22	13	110	120/70
23	Scirrhous	Yes	Yes	No	Yes	Exc.	1/2	A	20	20	14	105	120/68
								B	19	19	14	100	118/68
24	Scirrhous	Yes	No	No	No	Good	1/3	A	23	21	14	140	130/78
								B	23	21	14	130	124/68

* Side A indicates side operated on; side B, side not operated on; Exc., excellent.

of saline in the venous pressure between the two sides; in three of the eight the pressure was higher in the normal arm. Only two of the five patients with increased venous pressure showed measurable edema. Each of these two had only a minimal amount of edema (2 and 2.5 cm., respectively) and had excellent use of the arm. Four patients had had skin grafts; one of these (Case 11) had edema. Four patients, including the patient with the skin graft who had edema, had had a postoperative

infection, and subsequently measurable edema developed. None of these four patients had an increased venous pressure. Further, there did not appear to be any relation between edema and (1) the type of cancer, (2) x-ray therapy, (3) the presence of axillary metastases, (4) the arterial blood pressure, or (5) the use of the arm.

COMMENT

The only factor investigated that seems to be associated with the presence or absence of edema is infection. Thus, it appears probable that prevention of new lymph-channel formation through the process of infection and excessive cicatrization could well be the prime factor in causing the edema. The work of Hollenbach thereby becomes significant, in that the muscle graft may allow the early formation of lymph channels, extending from the arm to the chest wall, by bridging the resected area and reducing the amount of axillary scar tissue to a minimum. Treves [14] has recently reported the prevention of edema by (1) the use of Gelfoam rolls and (2) grafts of the teres minor muscle to cover the vein completely. Each of Treves's procedures produces the same effect as transplantation of the pectoralis minor muscle, namely prevention of excessive scarring by obliteration of dead space, but allows resection of the pectoralis minor muscle, as thought necessary for performance of complete radical mastectomy. Both Hollenbach's and Treves's procedures are based on Reichert's work demonstrating that minimal scarring allows early regeneration of the lymphatic channels.

SUMMARY

Increased venous pressure, presumably due to blockage of the axillary vein, does not seem to be an etiologic factor in postmastectomy edema; infection, with an increase in cicatrization, does seem to be a factor. Therefore the success of various vein-covering material, either natural or synthetic, is probably due to the successful obliteration of axillary dead space (which is particularly susceptible to infection and cicatrization), with the subsequent unhindered early formation of lymphatic vessels across the operative area.

14. Treves, N.: Prophylaxis of Postmammectomy Lymphedema by the Use of Gelfoam Laminated Rolls, Cancer **5**:73-84, 1952; Myolymphangoplasty for the Prevention and Relief of the Swollen Arm, Surg., Gynec. & Obst. **94**:65-69, 1952.

PRIMARY REPAIR OF MAJOR ARTERIAL INJURIES

Report of Fifty-Eight Battle Casualties

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PREVIOUS wars have demonstrated that approximately 1% of all battle casualties suffer damage to a major artery. Furthermore, of all amputations done on war wounded, 20% are the direct result of vascular injuries.[1]

The purpose of this study has been to assess the feasibility and value of primary repair to arterial wounds at the time of the initial definitive treatment at the forward field hospitals. This is therefore a report of results of primary repair at the mobile Army surgical hospitals, 8055 Army unit and 8209 Army unit, during the period from April through September, 1952.

Prior to the time of this study, many major arteries had been ligated. During the period mentioned above, only two patients, in whose care we participated, had a major artery ligated. These two patients could not be resuscitated sufficiently to permit a major operation. Both patients had ligations, and both survived. The first had a ligation of an axillary artery which resulted in an ischemic, but viable, extremity. The second had a popliteal ligation, and gangrene requiring amputation developed. With these two exceptions, the patients reported on represent successive unselected casualties. Minor arteries, especially those distal to the brachial and popliteal arteries, were frequently ligated, since the sacrifice of a single minor vessel rarely endangered the extremity.

It is fully realized that early operation in this group of casualties is desirable. However, as this represented a pilot study, patients were treated by arterial repair regardless of the time from wounding to operation. The lapse of time, or the time lag, therefore varied from 3 to 48 hours, with an average of 8.3 hours (Table 1).

The operation of election was always débridement with direct end-to-end suture anastomosis of the vessel. Two patients had small arterial lacerations (less than 20% of the circumference of the vessel). This permitted débridement followed by simple transverse suture repair. In all other instances it was necessary to excise

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Surgical Research Team of Korea (Major Jahnke and Captain Howard).

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1. DeBakey, M. E., and Simeone, F. A.: Battle Injuries of the Arteries in World War II: An Analysis of 2,471 Cases, Ann. Surg. **123**:534, 1946. Holmes, R. H.: Wounding Agent and Wound Ballistics, Symposium on Treatment of Trauma in the Armed Forces, Washington, D. C., March, 1952.

a complete cross section of the artery before any reparative type of operation could be employed. The defect was so large in eight patients that an autogenous vein graft was necessary.

The first principle of traumatic surgery being to control hemorrhage, it was found essential to gain control of the vessel before exploring the missile tract. This was routinely performed as the first step when arterial injury was suspected and led to a definite decrease in operative hemorrhage and vascular collapse.

The primary wound was then explored and the defect in the arterial tree located. Severed veins were usually ligated. Both the proximal and the distal end of the severed artery were débrided. The extent of damage was not always easily determined. Grossly roughened intima was considered a definite sign of damage, and débridement was carried beyond such an area to a point approximately 1 cm. into apparently normal vessel. Admittedly, such a criterion was, in part, empirical. The artery was freed proximally and distally so that approximation could be made without tension. Collateral circulation was sacrificed, as necessary, to permit attain-

TABLE 1.—*Time from Injury to Repair*

Time, Hr.	No. of Cases	No. of Amputations	% of Amputations
0-3	3	0	0
3-6	21	2	9
6-9	19	1	5
9-12	8	1	12
12-15	5	1	20
Over 15	2	1	50
Total	58	6	10.3

Average time lag 8.3 hr.

ment of this goal. The adventitia was then stripped away from the cut ends of the vessel in order to facilitate suture. Finally, the Potts principal clamps were momentarily released from the vessel ends to permit the free flow of blood, which cleared the artery of any residual clots. Anastomosis was then performed, using a continuous everting mattress suture of 5-0 braided nonabsorbable surgical (silk) suture material. Vascular clamps of the Potts type were used throughout this work.

When direct end-to-end suture anastomosis could not be performed without undue tension, an autogenous vein graft was inserted. The cephalic or saphenous vein was the most frequent vessel utilized as a source of the graft. In one patient this required transplanting and rotating muscle bundles, but this in no way made the procedure impracticable.

Arterial spasm in the proximal segment of the severed artery offered a technical problem in only five instances. In each of these, the same routine was followed. A sponge soaked in 2.5% papaverine hydrochloride solution was wrapped around the vessel, care being taken to cover the most proximal area of spasm. This sponge was left in place for 15 to 20 minutes and then removed. Spasm was thus relieved and could not again be induced in the treated segment of artery.[2]

2. Kinmonth, J. B.: Physiology and Relief of Traumatic Arterial Spasm, Brit. M. J. **2**:59, 1952.

Anticoagulant therapy was not used in this study. In view of the massive wounds so frequently associated with battle injuries, we felt its use was fraught with real danger.

After the completion of the vascular repair, the devitalized muscle was excised, and all other wounds were débrided. The skin and subcutaneous tissues were always left open. Postoperative sympathectomy was never utilized.

The extremity was immobilized in a split cast immediately after operation. Flexion of approximately 20 degrees was utilized in the elbow and knee joints to

TABLE 2.—*Results of Arterial Repair*

Artery	No. of Cases	Type of Repair			No. of Amputations
		Anastomosis	Graft (Vein)	Transverse Suture	
Common carotid	3	2	1	0	0*
Subclavian	1	0	1	0	0
Axillary	7	5	2	0	0
Brachial	16	15	1	0	0
External iliac	2	2	0	0	1
Common femoral	2	2	0	0	0
Superficial femoral	13	10	3	0	2
Popliteal	14	12	0	2	3
Total	58	48	8	2	6

* No neurological sequelae.

TABLE 3.—*Comparison of Amputation Rate After Primary Repair with Amputation Rate in World War II*

Artery	No. of Cases	Amputation Rate After Repair, %	Amputation Rate [1] World War II, %
Common carotid	3	0.0	30
Subclavian	1	0.0	28
Axillary	7	0.0	43
Brachial (above profunda)	4	0.0	55
Brachial (below profunda)	12	0.0	25
External iliac	2	50.0	46
Common femoral	2	0.0	81
Superficial femoral	13	15.0	54
Popliteal	14	21.0	72
Total	58	10.3	48

minimize tension on the suture line. Antibiotic therapy, consisting of penicillin and, occasionally, streptomycin, was used routinely. All patients were kept under observation at the mobile Army surgical hospital for from 7 to 14 days, depending upon whether an anastomosis or graft was performed.

RESULTS

The results of primary repair of arterial injuries are shown in Table 2. A comparison of these results with those following ligation in previous wars demonstrates beyond question the value of primary repair (Table 3). Several of the comparisons in Table 3 are statistically insignificant, but the over-all comparison is conclusive. Furthermore, such a study, in which amputation is the only end-result

being compared, fails to demonstrate the full value of primary repair. After ligation a markedly ischemic, functionally insufficient extremity frequently results. This syndrome has not been seen after primary anastomosis.

Long-range follow up is essential for complete evaluation of primary arterial repair. These studies have been instituted. However, analysis of the results to date permit several clinical observations. During the period of study, secondary hemorrhage has been observed only once. In this instance a secondary vein graft was successful. No other contraindications to early evacuation have been noted.

The six failures of primary repair resulted from two causes: first, irreversible damage preoperatively in the tissues of the extremity from ischemia, and, secondly, errors in operative technique. Four of the six failures resulted from an anastomosis (three cases) or a vein graft (one case) performed eight or more hours after injury. In three of these patients repaired 10, 13, and 14 hours after wounding, subsequent amputation below the anastomosis revealed not only gangrenous muscle but an actively spurting arterial circulation. In these three cases it would appear that irreversible changes had occurred in the muscle prior to the reestablishment of arterial continuity. In the patients successfully treated, a shorter time lag or a better collateral circulation prevented these irreversible changes.

The second factor leading to failure, technical error, centered primarily around the tension at the anastomosis site and, to an almost equal extent, around an inadequate débridement of the artery and of the surrounding tissue. In three instances, thrombosis occurred at the suture line. Two of these cases were associated with multiple (two) anastomoses at different levels in the same artery. Tension or inadequate arterial débridement, doubtlessly, was the underlying cause of failure. The sixth patient had a severe wound infection associated with devitalized muscle. Thus, time lag and thrombosis were the primary hazards of repair, with infection being of relatively minor significance. As a generalization, most of these complicating factors were probably preventable.

One patient died on the second postoperative day of an associated cerebral injury. This patient was among the six failures already described.

SUMMARY AND CONCLUSIONS

In the management of battle casualties the treatment of choice of arterial injuries is primary repair by direct end-to-end suture anastomosis or by autogenous vein graft.

Fifty-eight consecutive major arterial injuries were repaired by these techniques. Only six patients, or 10.3%, later required amputation of the involved limb, as compared with an amputation rate of 49% during World War II when ligation was the prevailing method of treatment.

Failures due to technical error were probably preventable, and infection was of relatively minor significance.

Although the percentage of successful anastomoses decreased after eight hours, the success of an individual anastomosis could not be predicted on the basis of time lag alone.

Further study is essential to delineate the limits of this mode of therapy.

The Medical Section, Far East Command, and members of the staffs of the mobile Army surgical hospitals, 8055 Army unit and 8209 Army unit, assisted and cooperated in this work.

TRYPTIC DÉBRIDEMENT OF CLOTTED HEMOTHORAX

Experimental and Clinical Study

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TRAUMATIC or postoperative hemothorax should be evacuated early to approximate the pleural surfaces, preserve pulmonary function, and obviate the need for surgical decortication.[1] There is always the possibility that clotting will take place despite early attempts at aspiration. Massive clotting has been reported as occurring in from four to six hours. Fibroblastic organization may begin as early as the fifth day. Experience in World War II indicated that from 15 to 20% of hemothoraces clot.[2] Organizing hemothorax occurs less frequently in civilian practice.

The lysis and aspiration of a clotted hemothorax by means of an enzymatic agent would be desirable. The intrapleural injection of crystalline trypsin has been shown to produce only minimal pleural and systemic effects in animals.[3] The proteolytic properties of trypsin are also well known.[4]

Experiments were conducted to determine the effectiveness of trypsin in the closed treatment of clotted hemothorax and also to observe any side-effects of wound healing.

EXPERIMENTAL METHOD

Thoracotomy and lobectomy were done on four dogs. Blood, 200 to 300 cc., was allowed to escape freely into the pleural space from the systemic circulation. It became apparent that this was not a standard condition of producing a clotted hemothorax when, upon simple aspiration 24 hours later, volumes approximating the original amount of hemorrhage were obtained. Accordingly a standard hemothorax was produced as follows. Blood was drawn into sterile beakers from donor dogs and covered and allowed to clot. These clots were refrigerated for at

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From the Department of Surgery, University of Kansas Medical Center.

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3. Reiser, H. G.; Roettig, L. C., and Curtis, G. M.: Tryptic Débridement of Fibropurulent Empyema, Forum (1950), 1951, p. 17. Roettig, L. C.; Reiser, H. G.; Habeeb, W., and Mark, L.: The Use of Trypsin in Chest Disease, Dis. Chest **21**:245, 1952. Reiser, H. G.; Patton, R., and Roettig, L. C.: Tryptic Débridement of Necrotic Tissue, A. M. A. Arch. Surg. **63**:568, 1951.

4. Dragstedt, C. A., and Wells, J. A.: A. M. A. Pharmacological Action of Trypsin, Quart. Bull., Northwestern Univ. M. School **18**:104, 1944. Dragstedt, C. A.: Digestion of Living Tissue by Proteolytic Enzymes, Science **98**:131, 1943.

least 24 hours. Well-formed serum-free clots weighing from 160 to 350 gm. were obtained. These clots were then placed by thoracotomy into the chests of 22 mongrel dogs. A clotted hemothorax was thus simulated with certainty.

Crystalline trypsin [5] was used for investigating purposes. In each instance a solution of 250 mg. of trypsin in 50 cc. of Sorenson's phosphate buffer was prepared immediately before use.

Preliminary in vitro studies were done to determine the proteolytic effect of trypsin solution on clotted dog blood. Clots weighing 250 gm. were incubated at 37 C. in 250 mg. of trypsin solution and were reduced in size by one-fourth in a 24-hour period without agitation. Control clots of the same weight, under identical conditions, but without added trypsin solution, failed to show any liquefaction.

The group of 22 dogs were divided into three series.

Series 1.—Twelve dogs were subjected to rib resection thoracotomy. A left lower lobectomy was performed on nine of these dogs. A preformed serum-free clot was placed in the chest of

TABLE 1.—*Thoracotomy with Instilled Clot Treated with Trypsin*

Dog No.	Weight of Clot Gm.	Total Dose of Trypsin		No. of Daily Injections	Total Aspirated, Vol. in Cc.	Fate Postoperatively	Postmortem Findings
		Mg.	Vol. in Cc.				
5	230	1,500	300	5	1,500	Killed, 15 days	Small fibrous cavity, 10 gm. clot
112	200	1,125	225	5	1,105	Killed, 7 days	Small fibrous loculation, 5 gm. clot
44	250	1,875	275	5	835	Killed, 25 days	Scattered adhesions, no clot
29	240	1,750	350	7	1,310	Killed, 49 days	Fibrous adhesions
51	175	750	150	3	225	Died, 4 days	Atelectasis and pneumonia, 45 cc. fluid, 15 gm. clot
57	225	250	50	1	Not done	Died, 36 hr.	Bronchopneumonia, 100 cc. fluid, 90 gm. clot
80	300	1,750	350	7	1,505	Died, 7 days	Atelectasis, 250 cc. fluid bilateral 4 gm. clot
27	250	750	150	3	160	Died, 4 days	Atelectasis and bronchopneumonia, 150 cc. fluid, no clot
7	230	1,250	250	5	1,100	Died, 6 days	Atelectasis, 200 cc. fluid, 35 gm. clot
38*	200	2,000	400	8	615	Killed, 36 days	Thin and thick adhesions
28*	350	2,000	400	8	1,100	Killed, 49 days	Thin adhesions
66*	300	500	100	2	150	Died, 3 days	Bronchopneumonia, 57 gm. clot, 340 cc. bilateral fluid

* All dogs except these had left lower lobectomy.

all 12 animals to simulate a clotted hemothorax. No attempt was made to pleuralize the bronchial stump when the lobectomy was performed. By this means an experimental condition similar to a clinical postoperative or traumatic hemothorax was produced. On the first postoperative day needle aspiration was done to determine if there was any spontaneous liquefaction. Prior to the daily intrapleural injections of 250 mg. of trypsin solution, 50 mg. of diphenhydramine (Benadryl [6]) hydrochloride was given intravenously.

The chest was aspirated just prior to each injection of trypsin solution and after the last treatment. Table 1 shows the animals in which lobectomy was done in order to simulate a postoperative hemothorax.

Although five animals in this series died from two to seven days after lobectomy, of pulmonary complications, this afforded an opportunity to observe the early effects of trypsin activity. In 10 dogs the original clot was reduced in weight from 91 to 100%. The two remaining dogs

5. Tryptar, a brand of crystalline trypsin, was supplied by Armour Laboratories, Chicago.

6. Rocha e Silva, M.: Concerning the Mechanism of Anaphylactic and Tryptic Shock, J. Immunol. **40**:399, 1941.

showed a residual clot of 20 to 40%. In general, the total volume of aspirated fluid after trypsin treatment exceeded in amount the combined columns of the injected trypsin solutions. The in vivo effectiveness of the trypsin solution is shown by a 90% reduction of a clotted hemothorax in one animal receiving daily injections (three injections) of trypsin solution (Dog 51). The six surviving animals, killed from 15 to 49 days, received a total of from five to eight daily intrapleural injections of trypsin. These animals showed expanded functioning lungs with little or no restriction by residual fibrous tissue. None of the 12 animals showed any evidence of impaired wound healing. All of the unpleuralized bronchial stumps showed varying stages of healing. Another proteolytic agent, streptokinase-streptodornase, has been used in the treatment

TABLE 2.—*Thoracotomy with Instilled Clot Untreated with Trypsin*

Dog No.	Weight of Clot, Gm.	Attempted Aspiration	Postoperative Fate	Findings
95	250	None	Killed, 14 days	Gross, brown "smudges" of mediastinal pleura; pigmented histiocytes, minimal interstitial fibrosis
24*	300	None	Killed, 21 days	Same as above
8	165	None	Killed, 16 days	Gross, fibrothorax; microscopic, well-developed thick fibrous tissue and organizing clot; pulmonary infarct and interstitial fibrosis

* This dog had lower lobectomy.

TABLE 3.—*Daily Intrapleural Injections of Trypsin in Control Dogs*

Dog No.	Total Dose of Trypsin		No. of Daily Injections	Total Aspirated, Vol. in Cc.	Disposition	Findings
	Mg.	Vol. in Cc.				
110	50	10	1 (right)	15	.....	Thoracoscopy done at 24 hr.; pleura glistening and normal; minimal serosanguineous fluid
110	250	50	1 (left)	None	.....	Thoracoscopy done at 24 and 48 hr. showed same finding as above
74	750	150	6	None	Killed, 7 days	Segmental atelectasis; 100 cc. bloody fluid in opposite untreated pleural space; spotty hemorrhagic areas
55	875	175	7	None	Killed, 39 days	Gross, lungs and pleura normal; microscopic, focal pleural thickening and interstitial fibrosis
43	875	175	7	None	Killed, 47 days	Gross, normal; microscopic, same as above
70	875	175	7	None	Killed, 55 days	Essentially same as above
78	875	175	7	None	Killed, 63 days	Gross, normal; microscopic, pleura showed minimal interstitial fibrosis and thrombosis

of clotted hemothorax.[7] Experimental studies also showed that this agent did not interfere with the healing of bronchial stumps or ligated vessels when pneumonectomy was performed with pleuralization.[8]

As to the early mortality of the six animals in this series, it should be noted that functionally the dog chest is one cavity.[9] The membranous pleura is thin and mobile in several areas. It

7. Sherry, S.; Tillett, W. S., and Read, C. T.: The Use of Streptokinase-Streptodornase in the Treatment of Hemothorax, J. Thoracic Surg. **20**:393, 1950.

8. Creech, O.; De Bakey, M. E., and Amspacher, W. H.: Effect of Streptokinase and Streptodornase on Wound Healing in Pulmonary Resection: An Experimental Study, S. Forum (1951), 1952, p. 25.

9. Graham, E. A.: Some Fundamental Considerations in the Treatment of Empyema Thoracis, St. Louis, C. V. Mosby Company, 1925.

is easily ruptured by air, blood, or free fluid in either chest cavity. It has been observed that air or fluid, even in small amounts, injected into one pleural cavity, may often pass to the opposite side although preexisting anatomical passages are not present.[10]

Series 2.—Preformed clots were placed in the chests of three dogs through a thoracotomy incision. One animal of this group had a lobectomy. Trypsin injections were not done. Repeated aspirations failed to produce any fluid. In this series of dogs with untreated hemothoraces, two, including the one with lobectomy, were killed at 14 and 21 days. The other two animals, when killed at 16 days, showed a well-developed fibrohemothorax (Table 2).

Series 3.—This group consisted of seven normal control dogs that received only intrapleural injections of trypsin. Bilateral thoracoscopy on one animal, after single injections of trypsin solution, showed only small amounts of a serosanguineous effusion. The pleura appeared normal after 24 to 48 hours. The remaining six animals received from six to seven daily injections of 125 mg. of trypsin and were killed at intervals up to 78 days. With the exception of one animal (Dog 74), killed at seven days, the lungs and pleura appeared grossly normal (Table 3).

Microscopic studies showed some minimal focal thickening of the pleura and slight interstitial fibrosis of the more superficial lung tissue. Observations on this series of animals without preexisting pathology indicated a minimal local tissue reaction to the intrapleural injection of trypsin. The majority of the animals in the above experiments which received intrapleural injections of trypsin solution showed objective evidence of chest pain. The pain occurred immediately after the injections and in some instances lasted for several hours. In some animals the chest pain appeared to be mild and transitory. In others the pain was persistent and severe in spite of intravenous injections of morphine or meperidine (Demerol) hydrochloride.

REPORT OF CASES

Crystalline trypsin proved to be an effective agent for the lysis of clotted hemothorax in dogs. Therefore a clinical trial was made on two patients.

CASE 1.—C. J., a 60-year-old, Negro man was admitted to the University of Kansas Medical Center on April 23, 1951. Two weeks prior to admission he had a spontaneous rupture of a syphilitic aneurysm of the ascending aorta. He had experienced no previous symptoms. Transfusion and thoracentesis had been done at two other hospitals. The bleeding had ceased spontaneously, and the patient was referred for definitive treatment. X-rays of the chest (Fig. 1 *A*) showed an opacity representing a residual clotted hemothorax on the right up to the sixth interspace, with the paralysis of the diaphragm on this side. The nonprotein nitrogen on the day of admission was 75 mg. per 100 cc. Multiple aspirations at different levels were attempted, and no free fluid could be obtained. Trypsin, 250 mg. in a 50 cc. solution, was injected into the right side of the chest. Prior to this treatment, 100 mg. of diphenhydramine was given by mouth one-half hour before treatment. Twelve hours after injection of the trypsin, 1,150 cc. of dark bloody fluid was aspirated; 250 mg. of the trypsin solution was injected on the two following days. Daily aspirations obtained 350 and 200 cc. of dark bloody fluid. No apparent untoward reaction was experienced by the patient. Expansion of the right lung was indicated by the postoperative x-rays and clinical signs (Fig. 1 *B*). A total of 1,700 cc. of aspirated bloody fluid was obtained over a three-day treatment period. The nonprotein nitrogen was then noted to be 48 mg. per 100 cc. On the fourth hospital day the patient had a right thoracotomy for a resection of the aneurysm. This gave us an opportunity to observe also the lung and pleural space on the right side. Only a minimal reaction of the visceral and parietal pleura was observed. This consisted of superficial disseminated hemorrhagic and fibrinous areas. There was 50 cc. residual clot-free fluid in the right pleural space. The point of rupture of the aneurysm on the anterior-superior aspect of the aorta was sealed over by the adherent lung.

Comment.—Crystalline trypsin produced an effective lysis of clotting hemothorax in this case but apparently did not interfere with the reparative process between the lung and the ruptured aneurysm. It is of interest to note that the azotemia improved after evacuation of the intrapleural hemorrhage.

10. Melick, D. W., and Spooner, M.: Experimental Hemothorax, J. Thoracic Surg. **14**:461, 1945.

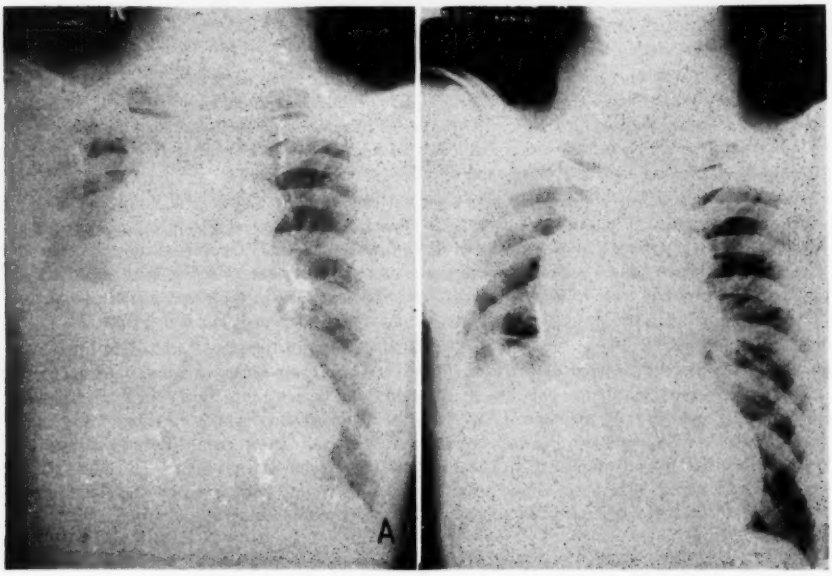

Fig. 1.—*A*, clotted hemothorax in right pleural cavity prior to trypsin treatment; *B*, appearance of chest two days after trypsin débridement of hemothorax.

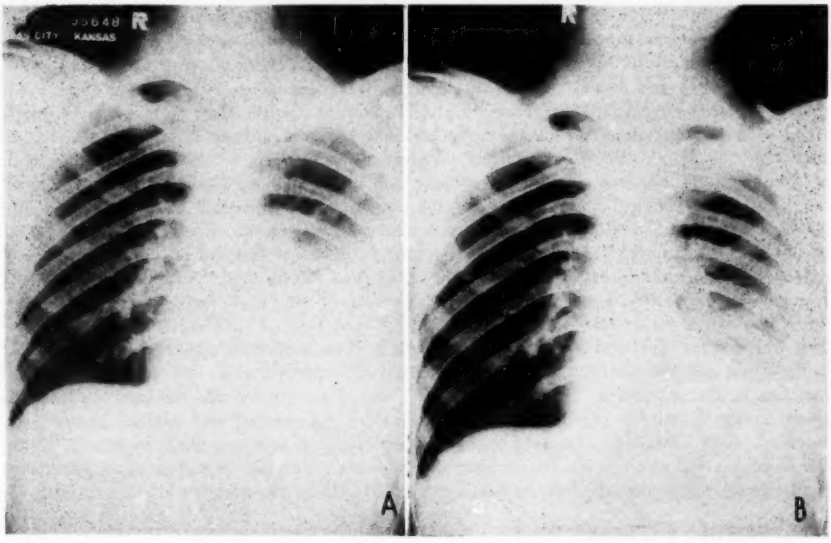

Fig. 2.—*A*, residual traumatic hemothorax in left pleural cavity three weeks after injury; *B*, appearance of left side of chest three days after trypsin débridement.

CASE 2.—D. K., a 20-year-old white woman, was admitted to the University of Kansas Medical Center on May 17, 1951. She injured the left portion of her chest three weeks prior to admission in an automobile accident. Immediate and protracted pain was present in the left side of the chest. Thoracentesis had been performed twice before admission, with removal of 600 cc. of blood. X-rays and physical finding showed a clotted hemothorax on the left (Fig. 2*A*). Multiple aspirations failed to obtain any fluid at various levels. Trypsin solution, 250 mg., was injected into the left pleural space. Prior to this injection, the patient received 100 mg. diphenhydramine by mouth one-half hour prior to the treatment. Immediately upon injection of the trypsin solution, the patient experienced severe pain in the chest which radiated down the left shoulder. Meperidine, 100 mg. administered intravenously, failed to control this chest pain. The intravenous injection of morphine sulphate, ⅛ grain (10 mg.), was given one-half hour later with no improvement of the chest pain. Eight and one-half hours after the injection of the trypsin solution, generalized abdominal pain and rigidity developed. There were no symptoms or signs of shock. It was thought that perhaps the original accident had also produced a small rent in the diaphragm. The lysis of the clotted hemothorax then allowed the residual trypsin solution to produce an irritation of the abdominal viscera. The abdominal rigidity and pain gradually subsided during the next two days. Twenty-four hours after the injection of the trypsin solution, a thoracentesis produced 850 cc. of bloody fluid. Repeated daily aspirations for the next three days obtained 300 cc., 30 cc., and 30 cc. A total of 1,210 cc. of bloody fluid was obtained after the one instillation of 250 mg. of crystalline trypsin. Clinically, breath sounds and expansion of the lung improved after treatment. X-rays also confirmed this observation (Fig. 2*B*).

Comment.—An effective lysis of the clotted hemothorax was obtained from one instillation of trypsin solution. This patient, however, had severe pain in the chest, as was observed in many of the experimental animals. The unusual reaction of abdominal pain and rigidity was an alarming, though not serious, complication.

Chest pain in the majority of the animals and in one patient was an undesirable side-effect. A series of 10 dogs were injected intrapleurally with 250 mg. of buffered trypsin solution, to which was added 10 cc. of 2% procaine hydrochloride. Daily injections were done for five days. Eight of these animals did not show any objective lessening of chest pain, as compared with those receiving trypsin solution alone.

Tetracaine (Pontocaine) hydrochloride was then selected because of its greater topical anesthetic effect to be injected intrapleurally prior to the instillation of the trypsin solution. Ten to twenty milligrams of tetracaine was used, depending upon the weight of the animal. Eight dogs receiving tetracaine intrapleurally 10 to 15 minutes prior to the instillation of the trypsin solution showed an objective absence of chest pain. No toxic side-effects from the intrapleural injection of tetracaine were observed in any of these animals.

SUMMARY AND CONCLUSIONS

Clotted hemothorax in the dog and in the pleural cavities of man may be spontaneously absorbed or be organized into a fibrous hemothorax. The intrapleural injection of trypsin solution effectively liquefies clotted hemothorax. There is an almost uniform undesirable side-effect of chest pain following the intrapleural injection of trypsin solution.

Experimentally there was no interference with the wound healing of the unpleuralized bronchus or ligated blood vessels. In the dog the addition of the intrapleural injection of tetracaine prior to trypsin injection proved to be an effective means of controlling chest pain.

ROENTGENOLOGIC DIAGNOSIS OF TRAUMATIC RUPTURE OF THE THORACIC AORTA

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RUPTURE of the aorta by a nonpenetrating injury is a major catastrophe that is almost never recognized during the time the patient survives the injury.

Any traumatic episode severe enough to rupture the aorta usually is instantaneously fatal or renders the patient in such a state of profound shock as to make impossible any detailed clinical investigation during his brief survival period. Occasionally the length of the survival period may be sufficient to permit certain reparative procedures to be undertaken, such as reduction of associated fractures and débridement, or suture of associated lacerations. It may be that the patient appears to improve strongly after the initial shock is overcome. Eventually, however, the patient dies, death coming after precipitous profound shock from which he cannot rally.

The sequence of events is easily understood. The initial injury must necessarily be of considerable compressing force to produce aortic rupture, if the aorta is normal. A logical assumption is that sclerosis of the aorta requires less force to cause aortic rupture. The rupture can be produced by an automobile steering-wheel compression or any similar severe blow to the chest. There should be evidence of thoracic-cage injuries, such as rib, sternum, spine, or clavicle fractures. There is often accompanying intracranial or intra-abdominal injury and fractures of the extremities. The size of the laceration of the aorta governs the degree of immediate mediastinal hemorrhage. If this laceration is small, an immediate brisk hemorrhage is followed by thrombus formation and temporary sealing of the laceration. This process is abetted by the hypotension of shock. Then after blood pressure returns to a more normal level, bleeding resumes. It reaches a lethal proportion either gradually by a steady unremitting hemorrhage or suddenly by massive hemorrhage. Rare, indeed, would be the patient who survives an aortic rupture.

Roentgenography of the thorax in rupture of the aorta (were it possible to obtain satisfactory films) should yield evidence of mediastinal fluid (blood), and this should be closely associated with the outline of the course of the thoracic portion of the aorta. Logically, so intimate should this association be that one should expect much distortion of the aortic outline, producing a widened, irregular, and indistinct mediastinal outline.

Certain aspects of cardiovascular surgery have now reached the stage of being reasonably routinized and standardized; other aspects are still in the midstage between laboratory experimentation and definitive clinical application. But such has been the progress of thoracic surgery that it is not crystal-gazing to predict that

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the traumatically damaged aorta may soon be reparable just as the congenitally deformed aorta is reconstructible. Although the present state of advancement of surgery may not be such as to allow every lacerated aorta to be repaired, even now this surgical feat is possible in isolated instances. Such surgical wizardry as a heart-lung mechanism for complete bypass of the heart and major vessels is not an unforeseeable reality. The repair of cardiovascular damage and the readjustment of complex congenital malformations and acquired abnormalities will then become possible, and even eventually commonplace.

It is therefore considered appropriate to report the following three cases of traumatic rupture of the aorta, in order to indicate the clinical features and to show the presence of certain roentgenologic features which permit the diagnosis to be

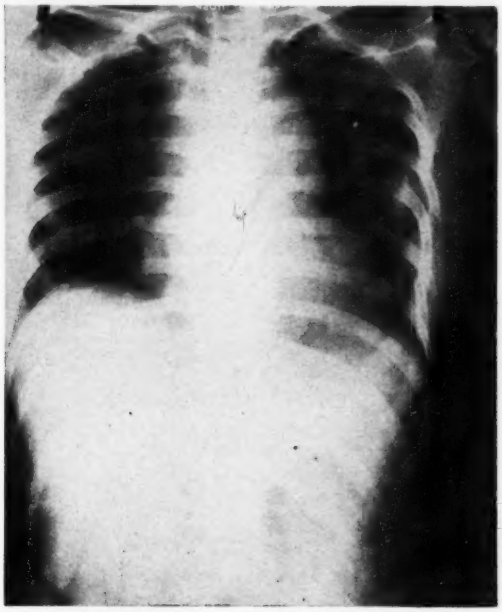

Fig. 1 (Case 1).—Roentgenogram of rib cage, showing fractures of first to seventh ribs, with overriding of fragments of the seventh rib. There is no pneumothorax or subcutaneous emphysema. Mediastinum is widened and trachea displaced to right.

made. We may then help clinical diagnosis to keep pace with surgical progress and give some chance for survival to such victims of an otherwise fatal accident.

CASE 1.—A 49-year-old white woman was admitted to Alexandria Hospital via the emergency room on Aug. 1, 1948, shortly after she was removed from the wreckage of a head-on collision between two automobiles. She was semicomatose on admission. The blood pressure was 115 systolic, 75 diastolic, pulse rate 95, and respirations 22 a minute. A large flap of the scalp of the right frontal area was avulsed. A generalized contusion of the left side of the thorax was present, with marked tenderness in the region of the fourth to sixth ribs posteriorly. Multiple contusions and lacerations were present over the face and the entire body. Physical examination of the chest was recorded as not remarkable. The blood count showed 3,000,000 erythrocytes, 9.5 gm. of hemoglobin per 100 cc., and 10,800 leucocytes, with 82% neutrophiles. A catheterized urine specimen was essentially negative. Plastic repair of the face and scalp was performed

shortly thereafter, and she was returned from the operating room in good condition. X-rays of the skull, dorsal spine, and left elbow revealed nothing abnormal. X-rays of the rib cage showed fractures of the left first to seventh ribs, with overriding of the fragments of the seventh rib. There was no pneumothorax or subcutaneous emphysema. The mediastinum was widened, and the trachea was displaced to the right (Fig. 1).

Later on the first hospital day her blood pressure rose to 170 systolic, 90 diastolic, with a regular pulse rate. Some decrease in breath sounds on the left side was noted. She required oxygen therapy for periodic cyanosis. For five days her general condition was unchanged, but thereafter she seemed to improve gradually, requiring only codeine for pain and barbiturates for sedation. On the eighth day she suddenly became worse, with a rapid thready pulse and an unobtainable blood pressure. A blood count showed 8.5 gm. of hemoglobin per 100 cc., 2,800,000 erythrocytes and 16,800 leucocytes, with 87% neutrophiles, with a shift to the left. Paradoxical motion of the left side of the thorax was observed, with very faint breath sounds. No cardiac

Fig. 2 (Case 1).—Bedside roentgenogram of chest, showing left hemothorax and some overriding of fracture edges of left ribs. Mediastinum is widened, with obliteration of normal outline of aortic arch.

murmur was heard. A bedside film of the chest showed a left hemothorax and some overriding of the fracture edges of the left ribs. The mediastinum was widened, with obliteration of the normal outline of the aortic arch (Fig. 2). She failed to rally and died on the eighth day.

Postmortem examination showed a huge hematoma of the mediastinum following the course of the esophagus from rupture of the thoracic aorta 5 cm. below the origin of the left subclavian artery. This was a transverse laceration 4 cm. in length through an arteriosclerotic plaque. The left pleural cavity contained 1,000 cc. of free blood, with the fracture edges of the left third and fourth ribs penetrating the left upper lobe.

Case 2.—A 51-year-old white man was admitted on April 4, 1949, after being struck by an automobile. On admission he was in shock, with the blood pressure 60 systolic and 40 diastolic, a large gaping laceration of the right shoulder and a compound fracture of the right leg. After the administration of 500 cc. of plasma, the blood pressure rose to 120 systolic, 80 diastolic. The shoulder wound was débrided and sutured and a drain inserted. The compound fracture of the

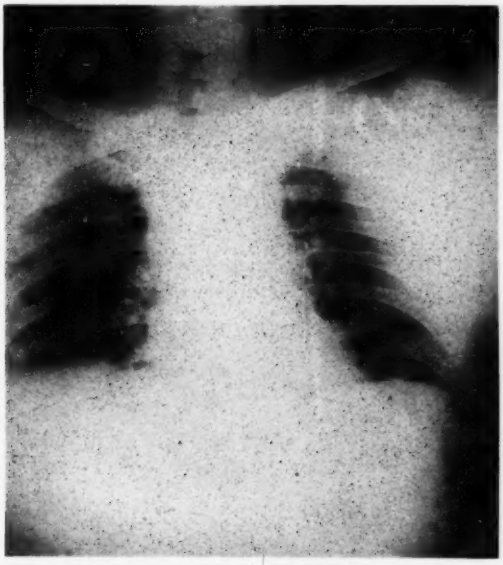

Fig. 3 (Case 2).—Bedside roentgenogram of chest, showing widening of upper mediastinal shadow with irregular density at level of aortic arch obscuring its normal contour.

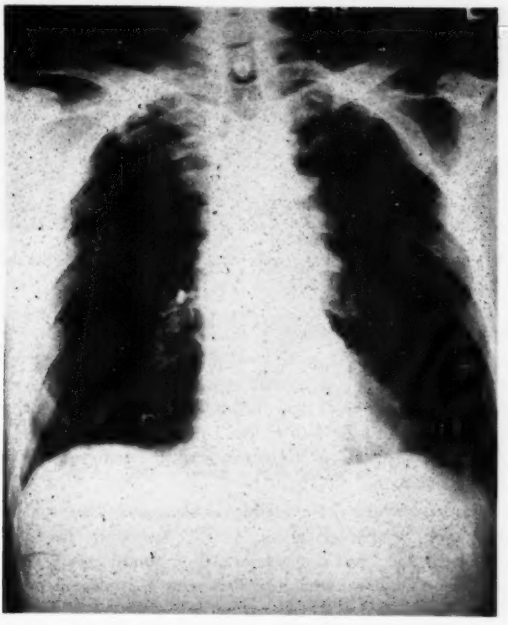

Fig. 4 (Case 3).—Bedside roentgenogram of chest showing widened upper mediastinum with irregular density at level of aortic arch obscuring its normal outline.

leg was cleaned and reduced, and a long-leg cast was applied. He was treated with penicillin, blood transfusions, and morphine for pain. Fourteen hours after admission the blood pressure suddenly fell to 80 systolic, 40 diastolic, and his pulse rate became rapid and thready, and respirations became labored. A bedside film of the chest showed widening of the upper mediastinal shadow with irregular density at the level of the aortic arch obscuring its normal contour (Fig. 3). He died 15 hours after admission.

Postmortem examination showed a complete transverse rupture of the aortic arch just above the pericardial reflexion, with a massive hematoma surrounding the rupture and massive mediastinal hemorrhage.

CASE 3.—A 91-year-old Negro man was admitted on Feb. 19, 1950, shortly after being struck by a speeding automobile. He had sustained a laceration of the scalp, a contusion of the anterior

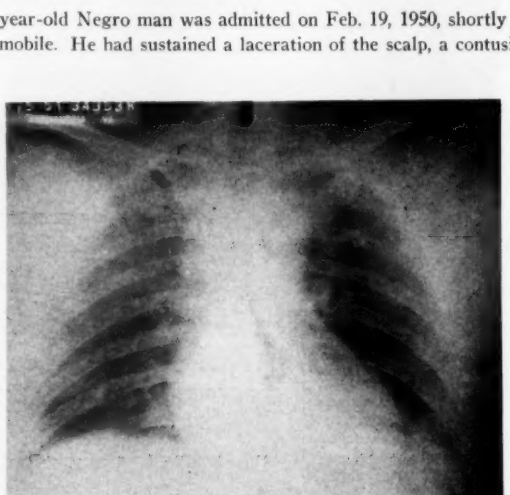

Fig. 5 (Case 4).—Roentgenogram of chest taken shortly after admission, showing indistinctness of aortic arch.

chest wall, and bilateral fractures of the leg. There was no evidence of intracranial injury. The blood pressure was 100 systolic, 68 diastolic, and, except for the fracture and lacerations, the physical examination was essentially noncontributory. The fractures were reduced and casts applied. He suddenly lapsed into coma nine hours after admission, showing fixed pupils and Cheyne-Stokes respiration. A bedside film of the chest showed a widened upper mediastinum with an irregular density at the level of the aortic arch obscuring its normal outline (Fig. 4). He died 11 hours after admission.

Postmortem examination showed extravasation of blood into the posterior mediastinal retropleural tissues and around the thoracic aorta. In the descending portion of the arch, 5 cm. beyond the left subclavian artery, was a sharp laceration almost completely around the circumference of the aorta. Surprisingly minimal atherosclerosis of the aorta was observed.

Comment.—The para-aortic density described for each of these cases is believed to represent the mediastinal hematoma found at autopsy. It is believed to represent

blood in different stages of coagulation caused by repeated or steady hemorrhage from the site of laceration. This blood will displace and compress the mediastinal surface of the lungs and add to the distortion, irregularity, and obscuration of the

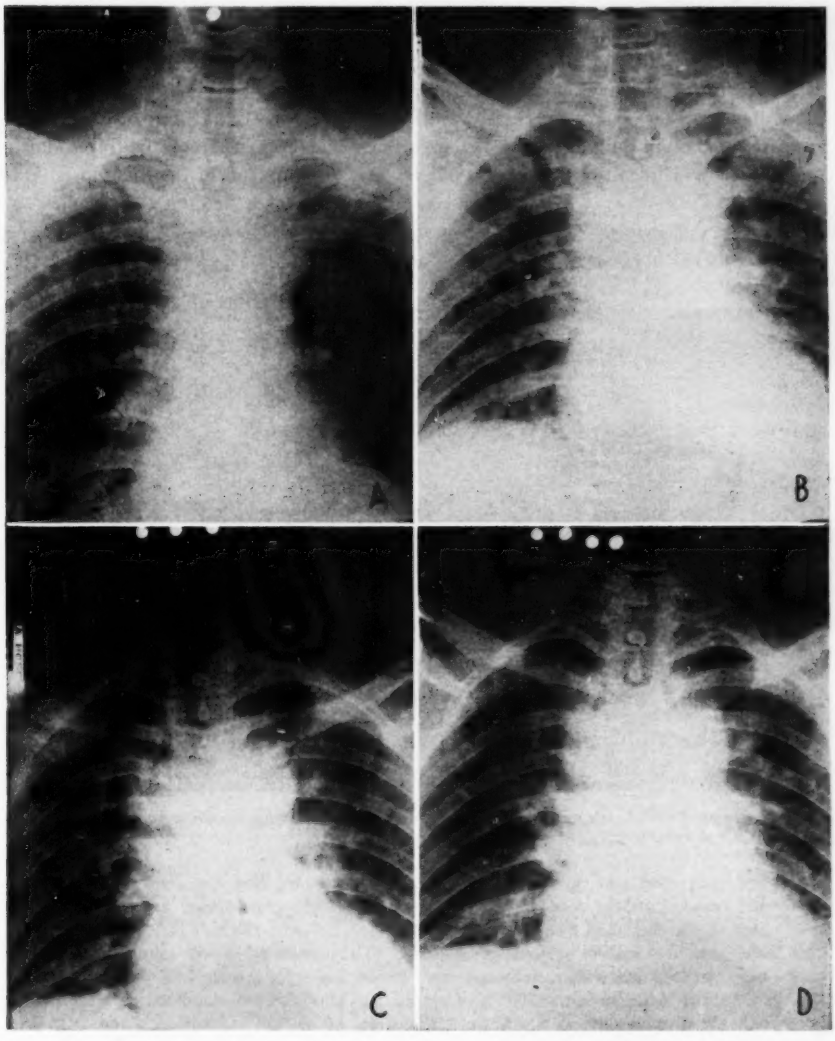

Fig. 6 (Case 4).—Serial roentgenograms of upper mediastinum taken at two (*A*), four (*B*), six (*C*), and eight (*D*) hours, showing progressive widening and indistinctness with suggestive layering of density at arch.

outline of the aortic arch. This effect can be demonstrated on bedside films and apparently does not require any special technique. On the original roentgenograms, there is definite indication of a "layering" effect surrounding the location of the

aortic arch, as if the outline of the arch is doubled or tripled by fluid and coagulated blood spreading along the aorta of the mediastinum.

The widened, distorted, and irregular outline of the aortic arch does not necessarily constitute a pathognomonic sign of aortic rupture. Such a finding may be present in mediastinitis, perforation of the esophagus, or mediastinal hemorrhage other than from a lacerated aorta. But this finding should be strongly indicative of traumatic aortic rupture when found following thoracic-cage trauma.

After the experience with these three cases and for the reasons stated above, the following case was very closely studied for the possibility of traumatic aortic rupture. Although this diagnosis was apparently incorrect, it is presented to indicate the mode of clinical and roentgenologic investigation once the diagnosis was entertained.

CASE 4.—A 49-year-old white woman was admitted on Feb. 15, 1951, after an automobile accident. She was the driver of a car which was struck on the left side, resulting in the driver's

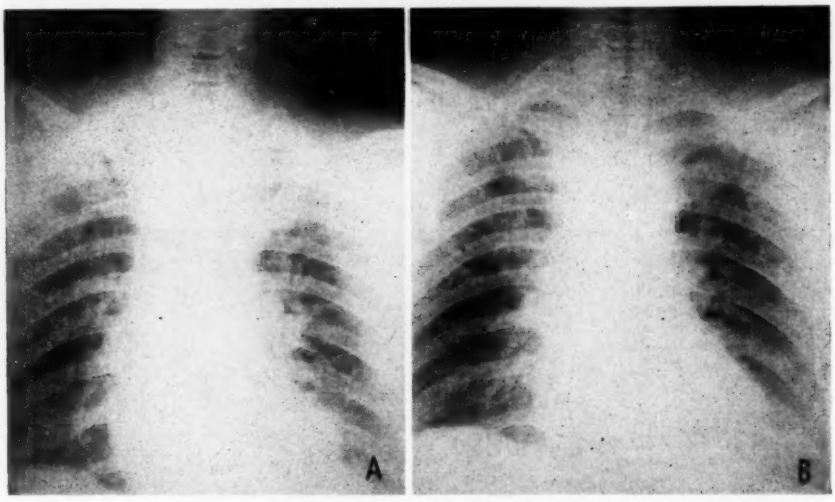

Fig. 7 (Case 4).—*A*, roentgenogram taken at 24 hours, showing some decrease in mediastinal widening; *B*, roentgenogram at 48 hours, showing still further decrease.

door being torn open and causing her to fall out of the car. She lost consciousness but on recovering crawled off the road and leaned against a telephone pole until aid came. She had severe pain in the chest and dyspnea at that time. On admission she was pale, cold, and moist. The blood pressure was 98 systolic, 80 diastolic. The peripheral blood showed 13.8 gm. of hemoglobin per 100 cc., 46% hematocrit, and 14,050 leucocytes, with 74% neutrophiles and 12% band forms. After an initial 500 cc. of plasma was administered, the blood pressure rose to 160 systolic, 90 diastolic, but slowly fell to 100 systolic, 60 diastolic four hours later. A "click" was heard over the anterior chest in the midline, synchronous with the heart and unrelated to respiration. A bedside film showed an undisplaced fracture of the left clavicle. This film one hour after the accident showed indistinctness of the aortic arch (Fig. 5). Serial films of the upper mediastinum taken at two, four, six, and eight hours showed progressive widening and indistinctness, with suggestive layering of the density at the arch (Fig. 6). A diagnosis of traumatic rupture of the aorta with mediastinal hemorrhage was made, and thoracic surgical consultation was obtained.

In the opinion of the consultant, the stabilization of the blood pressure, the steady full pulse rate, and the general satisfactory condition of the patient militated against the need for immediate

exploration. Thereafter the patient did well, with a gradual rise in blood pressure and a gradual disappearance of the mediastinal "click" on auscultation. A film in 24 hours showed some decrease in the mediastinal widening (Fig. 7 *A*) and in 48 hours still further decrease (Fig. 7 *B*). She recovered completely and was discharged in 13 days. Films of the chest three months later showed no mediastinal abnormality (Fig. 8).

Comment.—There was clinical as well as roentgenographic evidence of hemomediastinum in this case. That the hemorrhage came from a small aortic laceration is a matter for speculation, but it is considered highly unlikely. It is more probable that the findings were produced by blood from another source, particularly from injury to the internal mammary artery. This case, however, serves to emphasize the need for careful clinical study, whenever the type of trauma indicates that rupture of aorta is a possibility.

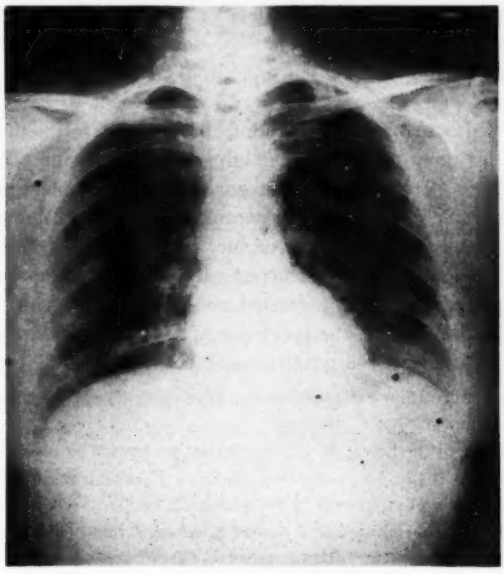

Fig. 8 (Case 4).—Roentgenogram of chest taken three months later, showing no mediastinal abnormality.

SUMMARY AND CONCLUSIONS

Traumatic rupture of the aorta from a nonpenetrating injury is almost never recognized while the patient is still alive and is almost always fatal. Occasionally such a patient may survive for a time, permitting appropriate clinical studies to be made.

The possibility of aortic rupture must be entertained whenever the thorax is involved in a compression injury or in any other severe traumatic episode. A bedside film of the chest is sufficient to demonstrate mediastinal widening, aortic arch distortion, and indistinctness.

It is important to make the diagnosis of aortic rupture as promptly and as accurately as possible because such a laceration may on occasion be repaired. Future surgical technical progress may be such as to prevent a fatal termination, provided criteria for the diagnosis are established and a diagnosis made promptly in each case.

SURVEY OF CURRENT OPINIONS CONCERNING CARCINOMA OF THE BREAST OCCURRING DURING PREGNANCY

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DALLAS, TEXAS

IT IS WELL recognized that carcinoma of the breast occurring in pregnancy has an unfavorable outlook. In fact, the results of treatment in the original series of cases studied by Haagensen and Stout at the Presbyterian Hospital, in 1943, were so uniformly discouraging as to cause them to conclude that radical mastectomy was unjustifiable in this group.[1] Although subsequent studies have led them to modify this point of view and to advise operations for pregnant women in whom the growth is not otherwise "categorically" inoperable, they have not yet encountered a "curable" case.[2] In an attempt to determine if the experiences of others with this problem was more favorable, a questionnaire was submitted to 55 persons who have been especially concerned with the problem of mammary cancers. Since my colleagues and I were interested not only in the results of treatment by radical mastectomy but also in the incidence of the disease and the advisability of auxiliary means of therapy, the questionnaire covered the following points:

1. How many cases of carcinoma of the breast developing during pregnancy have you seen? In how many was a "five-year cure" obtained?

2. Should carcinoma of the breast developing during pregnancy be considered inoperable.

3. In the premenopausal age, does pregnancy following a previous radical mastectomy increase the chances of development of carcinoma in the remaining breast?

4. Should pregnancy be terminated in a patient in whom carcinoma of the breast develops in the first trimester; second trimester; third trimester? Would you expect the five-year cure rate to be increased by the termination of the pregnancy?

5. Should sterilization or tubal ligation be done following radical mastectomy in the premenopausal woman to prevent further pregnancies?

SURVEY

Our interest was directed to the subject of carcinoma of the breast occurring in pregnancy by a personal experience. Because of the lack of information in the available literature on this subject, it was decided to follow the style of Trout and survey a representative group of physicians in this country and elsewhere. Among

From the Department of Surgery, Baylor University Hospital.

1. Haagensen, C. D., and Stout, A. P.: Carcinoma of the Breast: Criteria of Operability. Ann. Surg. **118**:859, 1943.

2. (*a*) Haagensen, C. D., and Stout, A. P.: Carcinoma of the Breast: Results of Treatment, Ann. Surg. **134**:151, 1951. (*b*) Haagensen, C. D.: Personal communication to the author.

the physicians selected were those who had written on the subject of carcinoma of the breast or who for other reasons were considered to have a special interest in the problem. The following replied to the questionnaire:

1. Ackerman, Lauren V, Washington University School of Medicine, St. Louis.
2. Bell, H. Glenn, University of California Medical School, San Francisco
3. Bowers, Ralph F., Veterans Administration Kennedy Hospital, Memphis
4. Brooks, Barney, Vanderbilt University School of Medicine, Nashville, Tenn.
5. Brunschwig, Alexander, Memorial Hospital, New York
6. Chenoweth, Arthur I., Medical Arts Bldg., Birmingham, Ala.
7. Clark, R. Lee, Jr., M. D. Anderson Hospital for Cancer Research, Houston, Texas
8. Cliffton, Eugene E., Yale University School of Medicine, New Haven, Conn.
9. Cole, Warren H., University of Illinois College of Medicine, Chicago
10. Copeland, Murray M., Georgetown University Medical Center, Washington, D. C.
11. Eckert, Charles, Washington University School of Medicine, St. Louis
12. Elman, Robert, Washington University School of Medicine, St. Louis
13. Farris, Jack M., 511 So. Bonnie Brae St., Los Angeles
14. Finney, George G., 2947 So. Paul St., Baltimore
15. Finney, J. M. T., Jr., 2947 So. Paul St., Baltimore
16. Foot, N. Chandler, Cornell University Medical College, New York
17. Foote, Frank W., Memorial Center for Cancer and Allied Diseases, New York
18. Geschickter, Charles F., 1834 Connecticut Avenue, N. W., Washington, D. C.
19. Glenn, Frank, and Cooper, W. A., New York Hospital, New York
20. Goode, John V., 2618 Oak Lawn, Dallas, Texas
21. Haagensen, C. D., Columbia University College of Physicians and Surgeons, New York
22. Harkins, Henry N., University of Washington School of Medicine, Seattle
23. Harrington, Stuart W., Mayo Foundation, Rochester, Minn.
24. Hart, Deryl, Duke University School of Medicine, Durham, N. C.
25. Hopkins, Frederick S., Westfield State Sanatorium, Westfield, Mass.
26. Horsley, Guy W., St. Elizabeth's Hospital, Richmond, Va.
27. Janes, R. M., and Peters, M. V., Banting Institute, University of Toronto, Toronto, Canada
28. Lewison, Edward F., The Johns Hopkins Hospital, Baltimore
29. MacDonald, Ian, University of Southern California School of Medicine, Los Angeles
30. McCleery, Robert S., Veterans Administration Thayer Hospital, Nashville, Tenn.
31. McGraw, Arthur B., Henry Ford Hospital, Detroit
32. McWhirter, R., The Royal Infirmary, Edinburgh, Scotland
33. Moyer, Carl, Southwestern Medical School of the University of Texas, Dallas, Texas
34. Orr, Thomas G., University of Kansas Medical Center, Kansas City, Kan.
35. Pack, George T., 139 E. Thirty-Sixth St., New York
36. Portmann, U. V., Cleveland Clinic, Cleveland
37. Sanders, R. L., Physicians and Surgeons Bldg., Memphis
38. Seybold, W. D., Hermann Professional Bldg., Houston, Texas
39. Shumacker, Harris B., Jr., and Lawrence, Edwin A., Indiana University Medical Center, Indianapolis

40. Slaughter, Danely P., University of Illinois College of Medicine, Chicago

41. Stanton, E. MacD., 146 Barrett St., Schenectady, N. Y.

42. Stewart, Fred, and Robbins, Guy F., Memorial Hospital, New York

43. Stone, Harvey B., 18 W. Franklin St., Baltimore

44. Taylor, G. W., 264 Beacon St., Boston

45. Trout, Hugh H., Jr., Jefferson Hospital, Roanoke, Va.

46. Wangensteen, O. H., and Hubbard, T. Brannon, Jr., University Hospital, University of Minnesota, Minneapolis

47. Womack, Nathan A., University Hospitals, State University of Iowa, Iowa City

A large majority of the 47 who answered the questionnaire commented on each of the five points presented. A small number offered no suggestions or opinions, and a like number did not reply to all questions. The questions that were asked were considered to be pertinent to the question of carcinoma of the breast occurring in pregnancy or related to pregnancy, and it was hoped that if the response were good we would be able to formulate some definite ideas that would aid in the treatment of the disease.

RESULTS OF SURVEY

1. *How many cases of carcinoma of the breast developing during pregnancy have you seen? In how many was a "five-year cure" obtained?*

There were 43 replies to this question. Instances in which the exact number of cases observed and the number of five-year cures were unknown have been omitted.

A total of 151 cases occurring in pregnancy had been seen personally. Eight five-year cures had been observed.

Thus the "five-year cure" rate was only 5.3%. Considering the large number of patients treated for cancer of the breast in the clinics represented by the persons to whom the questionnaires were directed, it was surprising to learn that cancer of the breast was seen so infrequently in pregnant women. This suggests that mammary cancer in pregnant women is an uncommon disease.

2. *Should carcinoma of the breast developing during pregnancy be considered inoperable?*

Thirty-seven replied to this question. None felt that pregnancy alone should be considered a factor which would render the tumor inoperable. All thought that, although the prognosis in this group is rather poor, an occasional case might be salvaged.

3. *In the premenopausal age, does pregnancy following a previous radical mastectomy increase the chances of development of carcinoma in the remaining breast?*

This question is one that is frequently asked. From a large group of surgeons, Trout had been able to collect 15 cases in which pregnancy had occurred after radical mastectomy for cancer of the breast. Of these cases, carcinoma had developed in the remaining breast in 13 patients. None had lived five years. He added two similar cases to this number.[3] Because of Trout's report we wished to see what had been the experience of others or their opinion on this point.

3. Trout, H. H.: The Remaining Breast After Radical Removal of the Opposite Side for Carcinoma, Surg., Gynec. & Obst. **34**:630, 1922.

Thirty-nine replied to this question. Eleven had no opinion. Twenty-two thought that a subsequent pregnancy did not play any role in the development of carcinoma of the remaining breast. Six thought that pregnancy did favor the development of carcinoma in the opposite breast.

4. *Should pregnancy be terminated in a patient in whom carcinoma of the breast develops in the first trimester; in the second trimester; in the third trimester? Would you expect the five-year cure rate to be increased by the termination of the pregnancy?*

Thirty-five replied to this question. Six stated that they had no definite opinion concerning this point. Ten thought that there was no reason to terminate the pregnancy. Nineteen replied that pregnancy should be terminated in the first trimester and of these 16 thought that pregnancy should be terminated in the second trimester as well as the first. Eleven of the 19 were of the opinion that the discovery of carcinoma of the breast at any time during pregnancy constituted an indication for interruption of the pregnancy. Of the group who thought pregnancy should be terminated, eight believed that the cure rate would probably be increased. The remaining 11 expressed no opinion.

5. *Should sterilization or tubal ligation be done following radical mastectomy in the premenopausal woman to prevent further pregnancies?*

Thirty-seven replied to this question. Seven had no definite opinion. Seventeen believed that sterilization or tubal ligation should not be done. Thirteen thought that one procedure or the other should be carried out.

COMMENT

No attempt was made to consider carcinoma of the breast developing during lactation, since the problem involved in this instance seems to differ significantly from that of carcinoma of the breast associated with pregnancy. It may be added parenthetically that the prognosis of the former appears to be more favorable than the latter.[4]

The factors influencing the unfavorable prognosis of mammary cancer occurring in pregnancy are not too well understood. Some of the ideas which have been presented [4a] will be briefly discussed.

1. Some observers have thought that the factor of age is of some importance, since the pregnant woman with cancer of the breast falls into the young or moderately young age group in which a higher grade of malignant growth is said to occur.[5]

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4. (*a*) Geschickter, C. F.: Diseases of the Breast, Ed. 2, Philadelphia, J. B. Lippincott Company, 1945. (*b*) Harrington, S. W.: Carcinoma of the Breast: Results of Surgical Treatment When the Carcinoma Occurred in the Course of Pregnancy or Lactation and When Pregnancy Occurred Subsequent to Operation, Ann. Surg. **106**:690, 1937.

5. (*a*) Harvey, S. C.: Indications for Therapeutic Abortion from the Point of View of the Surgeon, J. A. M. A. **137**:331, 1948. (*b*) Nathanson, I. T., and Welch, C. E.: Life Expectancy and Incidence of Malignant Disease: Carcinoma of the Breast, Am. J. Cancer **28**:40, 1936. (*c*) Taylor, G. W., and Wallace, R. H.: Carcinoma of the Breast, S. Clin. North America **27**:1151, 1947.

Others, however, doubt the importance of the age factor in prognosis, and it has been noted furthermore that there is no close correlation between the histological grade of the tumor and the survival rate.[6]

2. It is generally agreed that the rate of growth of the tumor is accelerated by the marked increase in estrogenic stimulation occurrig during pregnancy.[7] Geschickter has noted [4a] that the estrogenic level is high throughout pregnancy but thinks that the estrogenic effect on the breast may be diminished during the last half of pregnancy by an increase in the luteal hormone. Thus the unfavorable effects of increased estrogenic activity are apparently at a maximal level during the first half of gestation.

3. The increased fullness and size of the breast during pregnancy has been thought to make the detection of a mass, either by the patient or by the physician, much more difficult, so that in general the tumor at the time of discovery is already in an advanced state.[4a]

4. The increased vascularity of the mammary gland associated with the increase in size which occurs during pregnancy is thought to favor a more rapid dissemination of the growth.[4a]

At any rate, it is a well-established clinical observation that regional node metastases, as well as more distant ones, are much more commonly seen in the pregnant woman with cancer of the breast than in the nonpregnant one.[8] In fact, some writers emphasize the point that the clinical extent of the disease at the time of its discovery in the pregnant woman is, in the vast majority of cases, so advanced as to prohibit the possibility of cure by operation.[9]

This study would seem to indicate that carcinoma of the breast occurring in pregnancy is a relatively rare disease. The number of cases accumulated in the survey, 151, is surprisingly small considering the wide experience of the persons who answered the questionnaire. It should again be indicated that in a few instances, in which the exact number of cases seen was not stated, the answer was not considered suitable for tabulation. It is not believed that this omission significantly alters results. The totals listed in the results of the survey do not include the experience of Harrington at the Mayo Clinic, since his reply was not explicit enough to permit tabulation of his cases. Attention, however, is called to his paper of 1937 in which 92 cases of mammary cancer occurring in the course of pregnancy and lactation are reported.[4b] From a study of his tables it would appear that in 19 instances the growth developed during pregnancy. In an additional 11 instances operations were performed during pregnancy. Thus, in 30 cases the tumor developed or was removed at the time the patient was pregnant. In those patients

6. Orr, T. G.: An Attempt to Evaluate the Radical and Palliative Treatment of Breast Carcinoma, Surg., Gynec. & Obst. **90**:413, 1950. Warren, S., and Tompkins, V. N.: Significance of the Extent of Axillary Metastases in Carcinoma of the Female Breast, ibid. **76**:327 1943.

7. (*a*) Howard, W. J., Jr.: Carcinoma of the Breast: Present Status of Therapy, Am. J. Surg. **77**:696, 1949. (*b*) Scapier, J.: Pregnancy and the Development of Mammary Cancer, Am. J. M. Sc. **202**:402, 1941. (*c*) Geschickter.[4a] (*d*) Brooks, B., and Proffitt, J. N.: Influence of Pregnancy on Cancer of the Breast, Surgery **25**:1, 1949.

8. Haagensen and Stout.[1] Harrington.[4b]

9. Footnotes 1 and 2.

operated upon during pregnancy he was able to report a 75% five-year survival rate in the cases (4) without axillary metastases. None of the seven patients with axillary metastases present at the time of radical mastectomy lived five years. In the group (19) in which the tumor developed during pregnancy and operation was performed soon after its normal termination, he reported only a 6.2% five-year survival rate in those (17) with axillary metastases. The two without axillary metastases at the time of surgery lived five years and were free of recurrence of the disease. In his entire series, a 5.7% five-year survival rate is reported in the cases (78) in which axillary metastases were present at the time of radical mastectomy. A 61.5% five-year survival rate is reported for those cases (14) in which axillary metastases had not occurred. So far as can be determined, no other observers have been able to obtain comparable results; however, it should be noted that in Harrington's experience in instances in which lymph node involvement had occurred, the results obtained do not differ greatly from the results reported in the survey.

In contrast with the experience of Harrington, others have never seen a five-year cure. Among those whose experience with the disease has been uniformly unsatisfactory are Haagensen.[10] Lawrence,[11] Portmann,[12] Cole,[13] and Clifton.[14] Geschickter, while never personally having seen a permanent cure of carcinoma of the breast developing during pregnancy,[4a] has nevertheless studied sections from two cases in which the patients were free of disease after five years.[15]

It is the opinion of some that if the growth is confined to the breast the results of radical mastectomy may be fairly satisfactory. Unfortunately, however, instances in which the disease is not fairly advanced when first seen are quite infrequent. Authenticated reports of "five-year cures" by radical mastectomy in isolated cases have compelled the conclusion that pregnancy in itself cannot be considered to be a criterion denoting "categorical" inoperability.[2a] However, the improvement in the results of the surgical treatment of cancer of the breast has been due, at least in part, to a better evaluation of the clinical extent of the disease and to a more careful selection of cases for radical mastectomy. It has been noted that this "careful selection of cases for radical mastectomy is not an indication of timidity on the part of the modern surgeon, but rather an index of his knowledge of carcinoma of the breast."[10a]

The relationship of a subsequent pregnancy to the development of cancer in the remaining breast, following a previous radical mastectomy, remains a matter of doubt. The experience of Haagensen and Stout,[1] Brooks,[7d] and Harrington[16] causes them to believe that pregnancy is not an influential factor in the development of carcinoma of the breast. The majority of those replying to the questionnaire believed that the evidence implicating pregnancy to be inadequate. On the other

10. (*a*) Haagensen, C. D.: Carcinoma of the Breast, J. A. M. A. **138**:279, 1948. (*b*) Haagensen and Stout.[2]

11. Lawrence, E. A.: Personal communication to the author.

12. Portmann, U. V.: Personal communication to the author.

13. Cole, W.: Personal communication to the author.

14. Cliffton, E. E.: Personal communication to the author.

15. Geschickter, C. F.: Personal communication to the author.

16. (*a*) Harrington, S. W.: Personal communication to the author. (*b*) Harrington.[4b]

hand, attention should again be called to the report of Trout,[8] which notes that carcinoma of the remaining breast developed in 15 of 17 women who became pregnant after a radical mastectomy. Similar experiences of others have been noted by Horsley [17] and Howard.[7a] It does not appear possible at this time to reconcile this difference. Nathanson [18] has noted that "observations in human beings together with animal experiments strongly suggests that sex hormones are factors in the genesis and regulation of breast carcinoma." The effect of prolonged estrogenic stimulation on the development of mammary cancer has been demonstrated experimentally and a few cases in human beings have been reported in which this mechanism may be implicated.[19]

Many continue to advise any patient who has been subjected to radical mastectomy for mammary carcinoma to avoid a subsequent pregnancy. Some take this position because of their belief that such a pregnancy may increase the chance of cancer appearing in the opposite breast; others, because they think that the growth of any residual malignant tissue may be accelerated. In fact, because of the increased incidence of the development of carcinoma in the remaining breast, a few now recommend simple excision of the uninvolved breast at the time radical resection is carried out.[20]

Those replying to the questionnaire generally agreed that pregnancy should be terminated as soon as carcinoma of the breast is diagnosed, although several thought each case merited individual evaluation. A few emphasized the importance of considering the wish of the patient, or her family, in the matter. Cole [13] recognized the importance of religious objections in certain cases. Pack [20b] pointed out that the surgeon's religious belief regarding therapeutic abortions might influence his answer to this question and thought that an analysis of the replies received would be valueless unless this factor was considered. It did not seem advisable to resurvey the group and the results are offered therefore for what they may be worth without determining if religion influenced the reply.

It was generally agreed that if cancer of the breast is found in the third trimester, a viable baby may be obtained by either induction of labor or Porro Caesarean section, possibly accompanied by bilateral ovariectomy. A representative group thought that the "five-year cure" rate could be improved by the termination of pregnancy. It must be admitted that additional evidence will be required to verify this opinion. A contrary view is held by MacDonald,[21] who thinks that the cure rate would probably not be influenced because the "biological potential of the neoplasm is almost certainly determined before it is clinically apparent." Pack,[20b]

17. Horsley, G. W.: Treatment of Cancer of the Breast in Premenopausal Patients with Radical Amputation and Bilateral Oophorectomy, Ann. Surg. **125**:703, 1947.

18. Nathanson, I. T.: Hormonal Alteration of Advanced Cancer of the Breast, S. Clin. North America **27**:1144, 1947.

19. Haagensen, C. D.: The Surgical Physiology of the Breast, S. Clin. North America **29**: 1659, 1949. Waggoner, C. M.: Carcinoma of the Premenopausal Breast Endocrine Influence Suggested Clinically in 31 Cases, Ann. Surg. **127**:1256, 1948. Geschickter.[4a] Horsley.[17] Scapier.[7b]

20. (*a*) Hubbard, T. B., Jr.: Personal communication to the author. (*b*) Pack, G. T.: Personal communication to the author; (*c*) Argument for Radicalism in Cancer Surgery, Am. Surgeon **17**:271, 1951.

21. MacDonald, I.: Personal communication to the author.

Harvey,[5a] and others also feel that once the momentum of the disease is established termination of the pregnancy will have no influence on the ultimate outcome. Geschickter's experience with cancer of the breast following spontaneous abortions has led him to believe that the prognosis is better for such patients than for those in whom the pregnancy was not interrupted. Therefore he believes that therapeutic abortion should be done during the first two-thirds of the pregnancy if the disease is not already hopeless.[4a]

It is generally believed that women in the premenopausal group should avoid pregnancy for at least three to five years following radical mastectomy,[22] because its tendency to reactivate the growth of any residual tumor is well recognized. Although a majority of those replying to the questionnaire advised against subsequent pregnancy, only a minority thought that tubal ligation or sterilization by other means should be carried out. Most thought that the use of usual contraceptive measures would be adequate. Furthermore, the majority believed that castration should be reserved for patients with recurrent disease. Of those who advised sterilization, the majority thought castration, either surgically or by x-ray, to be the method of choice. More favored sterilization by x-ray than operation. Among the advocates of surgical castration were Horsley,[17] J. M. T. Finney, Jr.,[23] George Finney,[24] and H. H. Trout, Jr.[25] Those recommending castration do so with the belief not only that it will increase the five-year cure rate but also that the life expectancy of those who do not survive five years will be increased. In this connection the results reported by Horsley are of interest. He states that by routine employment of surgical castration he was able to increase the five-year cure in his series from 43.5 to 76.9%.[17] It might be pointed out that as early as 1896, Beatson,[26] and later Lett,[27] reported that surgical castration of women with inoperable mammary cancer seemed to retard the progress of the disease. Howard [7a] quotes Taylor as being unable to substantiate Horsley's results. It seems clear that further experience will be needed before the efficacy of surgical castration can be evaluated.

SUMMARY

A questionnaire dealing with problems relating to carcinoma of the breast occurring in pregnancy has been submitted to a number of physicians considered to be well informed on this subject. The replies have been tabulated and analyzed. Some features of the disease as it is seen in pregnancy are discussed, and some of the factors responsible for its poor prognosis are considered. The response to the survey indicates that the results of the treatment of carcinoma of the breast occurring in pregnancy are very disappointing.

22. Eckert, C., and Seaman, W.: Symposium on Clinical Surgery: The Palliative Treatment of Advanced Mammary Cancer, S. Clin. North America **30**:1435, 1950. Geschickter.[4a] Haagensen and Stout.[1] Harrington.[16a] Howard.[7a]

23. Finney, J. M. T., Jr.: Personal communication to the author.

24. Finney, G. G.: Personal communication to the author.

25. Trout, H. H., Jr.: Personal communication to the author.

26. Beatson, G. T.: On the Treatment of Inoperable Cases of Carcinoma of the Mamma: Suggestion for a New Method of Treatment, Lancet **2**:104, 1896.

27. Lett, H.: An Analysis of 99 Cases of Inoperable Carcinoma of the Breast Treated by Oophorectomy, Lancet **1**:227, 1905.

CONCLUSIONS

1. The prognosis of carcinoma of the breast developing during pregnancy, though poor, need not be invariably hopeless. Occasional instances of five-year cure have been reported. For this reason none of the respondents considered pregnancy to be a factor which in itself would cause the disease to be inoperable.

2. Termination of pregnancy in patients with cancer of the breast seems to be indicated, particularly if the growth is discovered during the first half of gestation and if there is no serious conflict with the religious tenets of the family.

3. There is general agreement that subsequent pregnancies should be avoided by women who have had mammary carcinoma. Most physicians thought that conventional contraceptive measures would be adequate and that operative sterilization was not advisable. A few observers were impressed with the value of surgical castration.

4. Whether pregnancy may increase the chances of carcinoma developing in the remaining breast remains an unsettled point. Most of those who replied to the questionnaire thought that it would not.

5. It appears that any hope for the improvement of the prognosis of carcinoma of the breast occurring in pregnancy lies in the recognization of the growth at any early stage when it is still clinically operable. For this reason obstetricians should be encouraged to examine the breasts of their patients carefully and at frequent intervals. It seems likely that instruction of the patients concerning techniques of examinations of their own breasts may be of considerable value.

USE OF POLYETHYLENE TUBING IN INTRAVENOUS THERAPY FOR SURGICAL PATIENTS

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AND
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MINNEAPOLIS

WITH THE advent of better anesthesia, the use of antibiotics, and improved operative techniques, surgical procedures of increased magnitude are now possible. As a consequence, preoperative and postoperative care has taken on a new and ever-increasing importance. Intravenous therapy is no small part of this care of the surgical patient.

Use of an intravenous needle over several days is traumatic, and it is difficult to retain the needle in position. Frequent clots occur, and phlebitis develops in the injured vein.[1] Extravasation of blood or fluids makes it impossible to find the vein again. In a short period, all of the superficial veins have lost their usefulness for intravenous therapy. The patient's partially or completely immobilized arm becomes a source of much physical anguish, and nursing care is increased and the patient cannot be moved without endangering the continuity of the infusion. Because of these well-known undesirable sequelae associated with the use of an intravenous needle, an effort has been made to evaluate the effects of using an indwelling polyethylene tube when parenteral fluids are to be given for more than a few hours.

The use of an indwelling intravenous polyethylene tube for the administration of fluids,[2] electrolytes,[3] vitamins, antibiotics,[4] transfusions,[3] and other drugs [5] offers a significant advance in the field of parenteral therapy, particularly when it is desired to continue the administration for more than a few hours.[6]

Polyethylene is the polymerization product of ethylene gas under high pressure.[7] It is a tough thermoplastic resin, which, because of its microscopically crystalline structure, can be cold-drawn like nylon. Polyethylene meets most of the require-

1. Horvitz, A.; Sacher, L. A., and Elman, R.: Experimental Study of Phlebitis Following Venoclysis with Glucose and Amino Acid Solutions, J. Lab. & Clin. Med. **28**:842-848, 1943. Tomarkin, J., and Strauss, A.: Venoclysis: Dangers and Contraindications, Am. J. Surg. **25**: 319-323, 1934. Tuell, S. W.; Martin, W. B., and Laufman, H.: Complications from Use of Plastic Intravenous Tubing, Quart. Bull. Northwestern Univ. M. School **22**:353-355, 1948.

2. Guenther, T. A.; Grindlay, J. H., and Lundy, J. S.: New Flexible Capillary Tubing for Use in Venoclysis, Proc. Staff Meet., Mayo Clin. **22**:206-207, 1947.

3. Farquhar, J. W., and Lewis, I. C.: Some Medical Uses of Polythene with Special Reference to Venoclysis in Infants, Lancet **2**:244-246, 1948.

4. MacQuigg, R. E.: New Techniques for Parenteral Fluid and Drug Administration, Surgery **18**:592-595, 1945.

5. McFadyen, W. A. L.: Heparin Administration by Polythene Tubing, Brit. M. J. **2**:925-926, 1949.

6. Zimmermann, B.: Intravenous Tubing for Parenteral Therapy, Science **101**:567-568, 1945.

7. Plastics Education Booklet, American Association of School Administrators, Nov. 1, 1945.

ments of a substance that can be satisfactorily buried in human tissue. It is nonabsorbable, unmodified by tissue fluid, chemically inert, nonepileptogenic in brain tissue, and noncarcinogenic.[8] It does not inactivate antibiotics, and it causes no tissue reaction unless it is incompletely cleansed of the diacetylphosphate which is retained from its commercial preparation.[9]

This plastic material was first used experimentally in the United States in 1941 by Simonds and Ellis.[10] Zimmerman [6] first used plastic tubing for infusion purposes in 1945.

Ingraham and his co-workers [8] studied tissue reaction in dogs, cats, and monkeys after polyethylene tubing and polyethylene film had been imbedded in the parietal lobe of the cerebral hemisphere. They found no gross reaction and no more microscopic reaction than was observed in a control stab wound.

Polyethylene tubes have been used as a dural substitute [11] for the repair of the common bile duct,[12] for obtaining blood [13] or for replacement transfusions through the umbilical cord in the newborn,[14] for continuous spinal, epidural, and caudal analgesia,[15] for ureterostomy catheterizations,[16] and for a variety of other purposes.[17]

Its commonest use has been in parenteral nutrition, wherein it has been used for the subcutaneous [18] and intravenous [19] administration of nutrient fluids.[20]

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PROCEDURE

In this series, polyethylene tubing was used in a wide variety of patients in order to evaluate the local and systemic reactions which might be encountered. The patients ranged in age from 6 to 90 years. The age of the patient was in no instance considered to be a contraindication to the use of the polyethylene tube.

It was used in 349 patients in whom 366 veins were catheterized. The type of case in which it was used is detailed as follows:

Type of Case	No. of Patients
Bowel obstruction	9
Appendectomy	65
Cholecystectomy	62
Gastric or bowel resection	52
Hernioplasty	38
Gynecological operations	35
Fractures	9
Thyroidectomy	7
Carcinomatosis	11
Intestinal bleeding	6
Malnutrition	4
Miscellaneous	51
Total	349

Needles and tubing of two different sizes have been used. For routine administration of parenteral fluid a thin-walled No. 18 gauge BD needle was used, through which a 24 in. (61 cm.) length of Clay-Adams polyethylene tubing was passed. This tubing has an inside diameter of 0.034 in. and an outside diameter of 0.050 in. When it is known that a large amount of whole blood might be infused, a No. 13 gauge thin-walled BD needle is used with a 24 in. length of Clay-Adams polyethylene tubing which has an inner diameter of 0.047 and an outer diameter of 0.067 in.

The needle is routinely autoclaved, whereas the tubing is cold sterilized for 18 hours or more in 1:1,000 aqueous benzalkonium (Zephiran) chloride solution.[21] In order to prevent coils in the tubing, sterization can be done in a tall glass jar. The tubing is then thoroughly washed in sterile isotonic sodium chloride solution before being used. Surgical asepsis and draping are used for the insertion of the needle and tubing.

The basilic vein just above the medial epicondyle is preferred, as this eliminates the kinking and bending of the tubing incident to elbow flexion, and it also eliminates the need for immobilization of the forearm. On some occasions the cephalic vein above the lateral epicondyle is used when the basilic vein cannot be entered. It is more difficult to thread the tubing into the cephalic vein, as this vessel usually takes a more acute angle at the shoulder, thereby preventing the tubing from passing into the larger subclavian or axillary vein. The femoral vein was used in eight instances and the jugular vein in one instance because the basilic or cephalic vessels had been obliterated by previous multiple needle infusions.

Before insertion of the needle the polyethylene tube is passed through the needle in order to insure a correct fit, as it is very disconcerting to insert the needle and find that the polyethylene tube will not pass through.

The needle and tubing are usually inserted while the patient is in the operating room and before he has awakened from the anesthesia. When the needle is inserted while the patient is in the ward, procaine hydrochloride (enough to produce a wheal) is injected intradermally in order to eliminate the pain associated with the insertion of a large needle.

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After the needle has been inserted so that blood is running freely, the tubing is threaded through the needle and into the vein. The tubing should be passed into the vein for a distance of 15 in. (38 cm.) or more.

After satisfactory insertion of the tubing, the needle is withdrawn over the tubing and firm pressure is held for a short time at the point of the needle puncture. If the tube is correctly placed within the vein, blood can be easily aspirated and reinjected. If this does not occur, the tubing is slowly withdrawn until blood can be easily aspirated. This maneuver releases any kinking that may have occurred as the tubing was passed up into the vein.

A single loose overhand knot is then tied in the redundant tubing, and this is strapped onto the arm or forearm. The tubing is then injected with isotonic sodium chloride solution in order to clear it of blood. This is done in order to prevent clotting of the blood within the tubing while the patient is being transported to his room or until the parenteral solution can be started. A 1 cc. syringe is attached to the tubing with a No. 19 gauge blunt-adapter needle. The patient's arm is not restricted. The patient is advised that she should not keep the arm in acute flexion as this occasionally obstructs the tubing.

RESULTS

The polyethylene tube was left in the vein for a period of from 1 to 42 days. Of the 366 veins catheterized, local reactions of one type or another occurred in 98 veins. Inflammatory reactions were found to occur in 16.66% of the veins catheterized. In addition, in 10.10% of the veins that were catheterized, what we considered to be a mechanical irritation developed. In these instances the patient complained of pain or discomfort, but no evidence of inflammation developed. The following reactions were manifest:

Inflammatory reactions		61 (16.66%)
Thrombosis	8	
Phlebitis	18	
Redness and swelling	4	
Pain and redness	31	
Local reactions		37 (10.10%)
Soreness or pain without redness and without evidence of inflammation	37	
Total		98 (26.77%)

No embolic phenomena were observed in any case. There was no slough and no abscess in any instance. In all those instances in which a local inflammatory reaction developed, it responded satisfactorily to the application of large hot packs and to the administration of penicillin.

Though these inflammatory reactions are undesirable, they were not considered alarming. It is recommended that the polyethylene tube be removed at the very first evidence of local reaction.

EFFECT OF PROLONGED CATHETERIZATION

It was considered that the length of time that the tube was in the vein might reflect, to some extent, the percentage of inflammatory reactions that were observed. To that extent the duration of continuous catheterization in those cases with inflammatory reaction were recorded. It was found that in those cases in which inflammatory reaction developed the tube was in the vein for an average of 3.9 days, as shown in Table 1.

In those cases with no inflammatory reaction but only a mechanical irritation, the polyethylene tube had been in for an average of 3.1 days, as indicated in Table 2.

In those instances in which there was no local reaction to the polyethylene tube, the catheter had been in for an average of 2.73 days (Table 3).

These findings seem to suggest that the duration of continuous catheterization contributes to the incidence of local inflammatory reaction in the vein.

In a few instances when it was considered that the tubing would be needed for a week or more, the addition of 10 mg. of heparin, as recommended by McFadyen,[5] to each liter of intravenous fluid made it possible for the tubing to remain in for an average of 8.5 days. Enough cases in this category have not been observed to determine whether or not this procedure should be routinely followed.

EFFECT OF BACTERIAL CONTAMINATION

Cultures were taken from the tip of the tubing in a number of cases. In every instance a culture yielding Staphylococcus aureus was found when an inflammatory

TABLE 1.—*Duration of Catheterization in Cases with Inflammatory Reaction*

Reaction	No. of Cases	Average No. Days
Thrombosis	8	5.0
Phlebitis	18	3.6
Swelling and redness	4	3.6
Pain and redness	31	3.89
Total	61	3.9

TABLE 2.—*Duration of Catheterization in Cases with Mechanical Reaction*

Reaction	No. of Cases	Average No. Days
Hardness (no redness or pain)	1	5.00
Soreness (no redness or inflammation)	21	2.76
Pain (no redness or inflammation)	11	3.54
Infiltration (no redness)	4	3.20
Total	37	3.1

TABLE 3.—*Duration of Catheterization in Cases with No Reaction*

Reaction	No. of Cases	Average No. Days
No reaction	268	2.73

reaction was evident in the vein. Cultures yielded no pathogens when there was no inflammatory reaction in the vein. This finding suggests that adequate sterility was not consistently maintained or that sterilization of the tubing in benzalkonium chloride solution was unsatisfactory.

It has also been considered that the microscopic to-and-fro motion of the tubing at the site of the puncture was probably the factor in introducing the infection from the skin. This contention has been arrived at on the basis that the appearance of a small red spot at the site of the puncture was uniformly followed by an ascending inflammatory reaction if the tube was allowed to remain in position for another 24 hours. The use of collodion, bacitracin ointment, or flamed tape at the site of the skin opening failed to reduce the incidence of inflammatory reactions.

It was further our observation that the type of solution which was used made no significant difference in the local vein reaction except in four instances in which a new solution was being tried.

LENGTH OF TUBING IN RELATION TO LOCAL VEIN REACTIONS

The length of the tubing residing in the vein was measured in 88 instances at the time when the tubing was removed. This was found to vary from 3.0 to 23.5 in. (7.6 to 58.4 cm.).

In 33 instances of inflammatory reaction, the average length of the tubing within the vein was found to be 11.9 in. (30 cm.), whereas in 55 instances of no inflammatory reaction the length of the tubing within the vein was found to average 14.43 in. (36.5 cm.).

In all instances the tubing was allowed to remain in the vein until it had served its purpose, or it was removed as soon as local reaction developed in the vein. In either case when the figures were cross correlated, it was consistently observed that the longer tubing allowed for a more prolonged period of catheterization before inflammatory reaction developed than did the shorter tubing.

PRECAUTIONS AND CONTRAINDICATIONS

It is recommended that in no circumstances should the tubing be pulled out through the inserting needle, as the sharp beveled edge of the needle may cut the tubing, leaving an irretrievable piece within the vein. This complication has not occurred in our cases.

Surgical asepsis and draping are recommended at all times, as the tubing may on occasion have a tendency to coil and swing out of control, thus becoming contaminated.

Though a polyethylene tube has been used in the femoral vein on several occasions and in the jugular vein in one instance, it is not recommended unless no other vein is available.

A small red spot at the site of puncture, pain, soreness, induration, swelling, and redness give, in this sequence, over a period of 24 hours, progressive signs indicating the need for removal of the tubing.

At the first of these evidences of reaction in the vein the polyethylene tube should be removed. It may be reinserted in the contralateral arm if additional parenteral fluids are needed. In this manner we have been able to avert the development of a definite thrombophlebitis in many instances.

CONCLUSIONS

These studies on 349 patients would seem to suggest that when polyethylene tubing is used for the administration of parenteral fluids it should be inserted for a distance of 15 in. (38 cm.) or more; it should be removed at the very first sign of local reaction, which is evidenced as a small red spot at the site of entrance.

These studies indicate that the use of polyethylene tubing is feasible in those instances in which parenteral fluid is needed for more than a few hours.

ADDENDUM

Since presenting this paper for publication we have used 10 mg. of heparin in each liter of solution throughout the period of infusion in 16 cases. The average length of time in which the tube was left in was six days, without reaction. The incidence and types of reactions were essentially the same as reported above.

The 10 mg. of heparin in each liter of parenteral solution has not been sufficient to cause any alteration in the coagulation of the blood in these cases.

Case Reports

ANOMALOUS POSITION OF THE GALL BLADDER WITHIN THE FALCIFORM LIGAMENT

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ROBERT L. SCHMITZ, M.D.
AND
STRAVRULA PERUTSEA, M.D.
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AMONG the congenital anomalies of the gall bladder are those of position. The following anomalous locations have been reported: intrahepatic,[1] attached to the left lobe of the liver,[2] free-floating,[3] retroperitoneal,[4] and within the abdominal wall.[5] In situs transversus, the gall bladder will, of course, be left-sided, but its relation to the liver and hepatoduodenal ligament will be otherwise normal.

No report has been found by us of a case similar to the one to be reported.

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Assistant Clinical Professor of Surgery, Stritch School of Medicine, and Associate Attending Surgeon, Mercy Hospital (Dr. Schmitz).

Resident in Surgery, Mercy Hospital (Dr. Perutsea).

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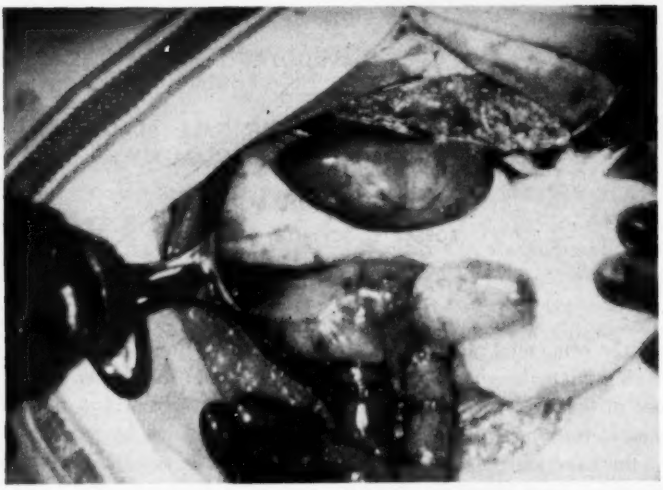

Fig. 1.—Gall bladder suspended within falciform ligament and mucocele of the appendix.

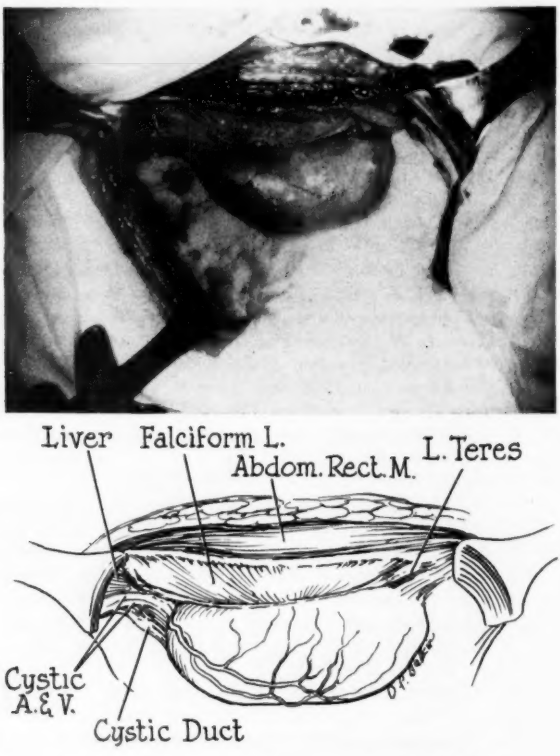

Fig. 2.—Anatomical details of anomalous gall bladder.

REPORT OF A CASE

A 36-year-old Negro man reported to the Mercy Hospital free dispensary on Oct. 26, 1951, for treatment of asthma, which he had had for eight years. Except for his respiratory complaints, a system review was negative, nor had he had any significant illness in the past. His mother died at age 66 of some type of gall-bladder disease, but the details were unknown to the patient.

Physical examination revealed a well-nourished and normally developed Negro man. Musical rales were heard throughout both lung fields on inspiration and expiration. In the middle of the right lower quadrant of the abdomen a mass was palpable. It was ovoid in shape, about 8 by 3 by 3 cm. in size, solid, discrete, freely movable and nontender; it tended to slide away from beneath the fingers but would resume its former position when pressure was released.

Complete blood count, urinalysis, reaction to the Kahn test, and roentgenogram of the chest revealed nothing abnormal. Barium enema studies of the colon were normal; the cecum filled well; the appendix was not visualized.

On several subsequent examinations, the mass was again palpated. A diagnosis of mucocele or carcinoid of the appendix was suggested, and surgical exploration was advised.

A lower right rectus muscle-splitting incision was made. Exploration revealed a mucocele of the appendix, but there was, also, a cystic pear-shaped structure dangling within the falciform ligament (Fig. 1). Extension of the incision upward revealed the following: The gall bladder, normal in size, shape and color, was suspended in its entirety within the leaves of the falciform ligament (Fig. 2, upper). The fundus was 2 cm. from the umbilical attachment of the ligament, and the ampulla was 3 cm. from the liver edge. The ligamentum teres ran in normal position along the undersurface of the liver, entered the falciform ligament at the liver edge, and continued in it between the abdominal wall and the gall bladder to the umbilicus (Fig. 2, lower). In the free edge of the falciform ligament were the cystic vessels and between them and the ligamentum teres, the cystic duct. These structures were approximately 9 cm. in length; at the liver edge they veered laterally to what should have been gall-bladder fossa, taking a thin fold of falciform ligament with them, and thence toward the hilus of the liver to enter the hepatoduodenal ligament. The cystic duct joined the common duct at a right angle, and the vessels continued on another 0.3 cm. before veering medially to join the right hepatic artery and the portal vein.

A cholecystectomy and appendectomy were performed. The gall bladder measured 8.5 by 2.5 cm. in its greatest dimensions and the amputated cystic duct and vessels 8.0 cm. in length. The gall bladder contained 30 cc. of golden-green bile. The mucosa was normal, and no stones were present.

The appendix measured 9.5 by 3.5 cm. in its greatest dimensions, and the distal seven-eighths of the organ was replaced by a doughy swelling, the cut surface of which was pale yellow and mucinous. The microscopic sections were compatible with a diagnosis of mucocele.

COMMENT

A review of the embryological development of the gall bladder suggests no ready explanation for the abnormal location of that organ in this patient.

SUMMARY

A previously undescribed anomalous location of the gall bladder within the falciform ligament is reported.

RELIEF OF CARDIAC FAILURE BY SURGERY IN AN INFANT WITH COARCTATION OF THE AORTA

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IN INFANCY coarctation of the aorta is a common cause of cardiac failure.[1] Management of the associated decompensation of the heart is unusually difficult, and the prognosis is poor. Surgical correction of this anomaly should be done when it is evident that medical treatment is unsatisfactory. The following report describes such a case in a 16-month-old child with a two and one-half year follow-up after successful surgical repair.

REPORT OF A CASE

D. M., a white girl, was born at term at another hospital on Nov. 6, 1948. She weighed 7 lb. 11 oz. (3.5 kg.) and was apparently normal. At 14 days of age she was readmitted to the same hospital seriously ill. She had seemed well until the day before when a cold developed. The next morning she refused her formula and that afternoon became dyspneic. Examination revealed a pale grayish cyanotic baby with rapid respiration and temperature 102 F. but no rales in the lungs. The heart was enlarged to percussion, with a rate of about 190 beats a minute and a regular rhythm. No murmurs were heard. The liver was palpable 4 or 5 cm. below the costal margin, and chest x-rays revealed the heart to be enlarged to the left. The patient was digitalized, put into an oxygen tent, and given penicillin. Improvement was so rapid that by the third hospital day she no longer required oxygen, and on the fifth day there were no signs of failure; consequently use of digitalis was discontinued. She was discharged on the seventh hospital day.

She was well until age 2½ months when another respiratory infection developed followed by signs of heart failure. She was admitted to Duke Hospital. Again she responded dramatically to penicillin and digitalization. The electrocardiogram on the day of admission showed a rate of 136 beats a minute; P-R interval, 0.12 sec.; QRS, 0.07 sec.; diphasic T_3 and inverted T_3 with no axis deviation. A repeat electrocardiogram two days later was interpreted as showing left axis deviation with elevation of ST_2 and ST_3. X-rays of the heart showed left ventricular enlargement. She was discharged at the end of 10 days, being given 0.03 gm. of digitalis leaf each day. This was continued throughout the first 16 months of life. The cause of the poor cardiac reserve was not understood at this time.

At the age of 3 months, a systolic murmur was noted over the entire precordium, loudest in the aortic area and transmitted to the back. The heart rate was 90 beats a minute, and there was no evidence of cardiac failure. At 5 months of age, her blood pressure, using a 2.5 cm. cuff, was recorded as 100/50 in the right arm and 120/50 in the left arm. Her course throughout the remainder of the first year was characterized by slow growth, irritability, and frequent severe upper respiratory infections. At 1 year of age she weighed 16 lb. 2 oz. (7.4 kg.), had been sitting for several months, and seemed to have normal intelligence.

From the Division of Thoracic Surgery and the Department of Pediatrics, Duke Hospital.

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On reevaluation at 15 months of age, the patient was found to have a blood pressure of 230/120 in the right arm and 235/120 in the left arm, using a 7.5 cm. cuff. The pressure in the right leg was 130/100, and femoral arterial pulsations could just be felt. It was only at this time that the cause of the failure was appreciated, and the diagnosis of coarctation of the aorta was made. The mother stated that the child did not play and tired easily. It was also noted that the patient had an unusual habit of trying to stand on her head during periods of irritability. The electrocardiogram showed a rate of 167 beats a minute, with no axis deviation. ST_2 and ST_3 were less upright than previously, and T_2 and T_3 were taller. Q_2 and Q_3 had appeared, and T_4 was upright. Fluoroscopy and x-rays of the chest showed enlargement of the left ventricle. In view of the extremely high and increasing pressure in her upper extremities, as well as the evident

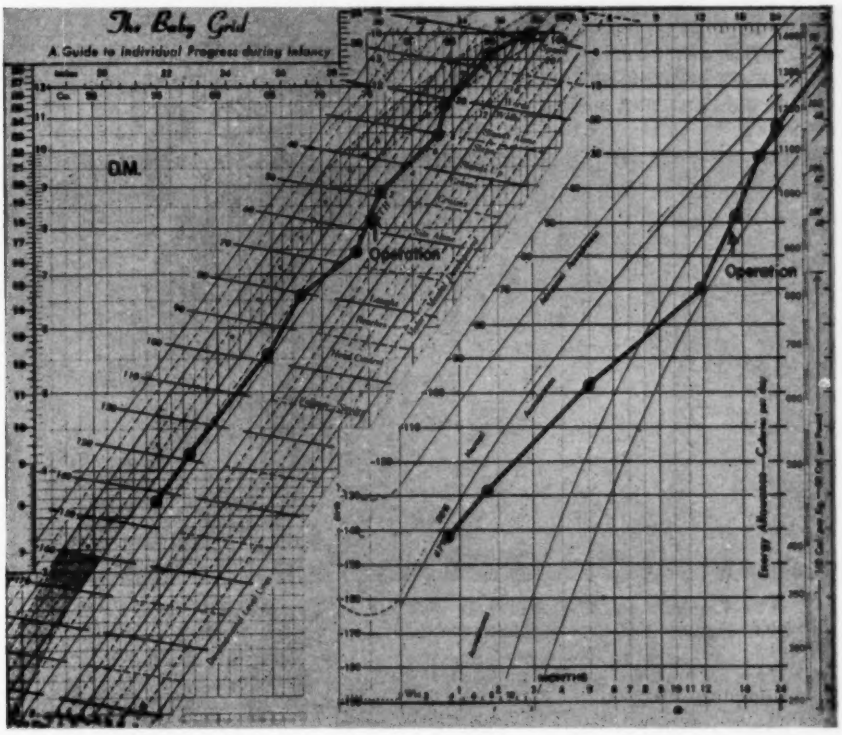

Fig. 1.—Effect of operation upon growth (Wetzel baby grid). Graph on left shows change of body build from slender type (A_5 channel) preoperatively to average type (A_8 channel) postoperatively. Graph on right shows that during infancy, D. M. changed from her original normal auxodrome to the premature position preoperatively. Normal auxodrome was regained within one year after operation.

poor cardiac reserve and retarded development even on strict medical management, excision of the coarctation of the aorta was deemed advisable at this age.

At 16 months of age, the chest was explored through a left posterior lateral incision. The extent of the collateral circulation on the chest wall was striking. There were numerous large, tortuous, friable arteries in the subscapular area. The intercostal arteries were typical of those seen in an adult with coarctation. The aorta was found to be narrowed from a point just below its junction with the left subclavian artery. The left subclavian and internal mammary arteries were tortuous, enlarged, and thin walled. The entire aortic arch appeared to be dilated. A large

ligamentum arteriosum was identified attached to the aorta about 1.5 cm. below the arch. Just below this point there was a hard firm nodule in the aorta, and no thrill could be felt in the aorta below this area.

The aortic arch and first portion of the descending aorta were mobilized. Then a section of the aorta, 1 cm. in length to include the stricture, was resected. The aorta was noted to be completely occluded at the stricture site. The two ends of the aorta were approximated by means of interrupted 00000 nonabsorbable surgical (silk) sutures.

After the completion of the suture line, the upper and lower clamps were removed, but because of bleeding, it was necessary to reapply the clamps. At this time bradycardia occurred followed by momentary cardiac arrest. After administration of blood, atropine (0.2 mg. intravenously), and cardiac massage, the heart action and blood pressure were restored to normal. Then another interrupted suture was placed in the wall of the aorta. This adequately controlled the bleeding from the suture line.

The child's postoperative course was uneventful. On the ninth postoperative day her blood pressure was 160/80 in both arms (7.5 cm. cuff) and 190/140 in the legs. Arterial pulsations in the legs and the arms were normal.

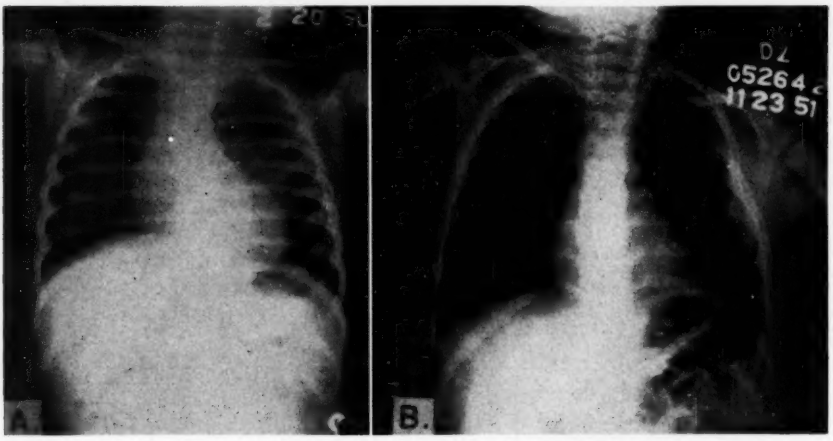

Fig. 2.—Posteroanterior chest x-rays: *A*, showing configuration of heart at 16 months of age; *B*, configuration of heart 21 months after operation.

She has been followed for two and one-half years since operation, and her course has been surprisingly good. The blood pressure in the arms has remained about 150/80-0 (7.5 cm. cuff). The femoral arterial pulsations have remained normal, but due to poor cooperation it has been difficult to obtain good leg blood pressure readings. One month postoperatively a reading of 160/110 was obtained in one leg, but more often it has been around 120/80. Her change in disposition from a fretful child to a happy one has been most striking. Her weight gain and change in growth pattern were also interesting. During the first year after operation she gained from 19¼ to 27¾ lb. (8.8 to 12.5 kg.) and at age 3 years and 3 months weighed 30 lb. (13.6 kg.) (Fig. 1). The systolic murmur at the base of the heart became slightly louder and more constant postoperatively, and there was a loud continuous hum in the right interscapular region which may be due to the collateral circulation. A soft diastolic murmur has been heard over the aortic area at times. Fluoroscopy and chest x-rays done 20 months postoperatively showed diminution in size of the left ventricle (Fig. 2). She has not required digitalis since operation in spite of greatly increased activity and several respiratory infections with high fever. Three years after operation her condition was excellent, with the blood pressure remaining in the range of 150/80 in the arm.

COMMENT

The change in this child from a fretful sickly one to a happy one has been most gratifying. She has by accelerated growth rate regained her original auxodrome on the Wetzel baby grid (Fig. 1). The reduction in the heart size and the ability of the patient to remain compensated without digitalis demonstrate that by removal of the aortic stricture a great load has been removed from the heart.

The explosive onset of the cardiac decompensation in this case at age 2 weeks was dramatic. Bahn, Edwards, and DuShane[2] have explained the heart failure in infants with coarctation on the basis of a lack of collateral vessels around the strictured area. If *in utero* the ductus enters either below or adjacent to the stricture in such a way that there is a large volume of blood coursing down the distal aorta, according to these authors, there would be no stimulus to the formation of collateral circulation. The location of the ligamentum arteriosum in our case did not rule out Bahn, Edwards, and DuShane's theory.[2] The progressive hypertension and the poor cardiac reserve in the presence of large and apparently adequate collaterals can be assessed as evidence against this theory. The blood pressure recordings at age 5 months revealed a pressure of 120/50 in the arm, while at 15 months the pressure had increased to 230/120. The experience[3] with experimental coarctation in dogs indicates that after about two weeks of constriction the pressure becomes elevated. Then in nine months to a year there is a fall in the blood pressure, not to normal, but much below the maximum elevation. The latter change is thought to be the result of the formation of collateral circulation. In this case the trend in the blood pressure was upward when there must have existed adequate collaterals.

The explanation for the cardiac failure in this child with coarctation is not at once evident. The number and size of the collaterals would seem to indicate that adequate vascular pathways existed for lower body needs, so that, even in the face of complete aortic obstruction, failure should not have occurred. The only clue that some other circulatory defect might be present and by additive effect cause cardiac failure has been the persistently high pulse pressure observed in the postoperative period. Though other clinical signs do not confirm this, aortic insufficiency due to a bicuspid valve could be the cause of the elevated pulse pressure. On the other hand, a slight narrowing of the aorta at the site of the anastomosis or widely patent large collaterals could give this change in the pulse pressure.

The problem of failure of growth of the aorta at the site of anastomosis is always interjected into any consideration of the treatment of coarctation in infants and young children. In instances in which the patient's condition is such that surgical relief is imperative, the future change in size is not of great importance. It is highly probable that the anastomotic site will increase enough in size to allow for adequate flow through it, even in adult life, as there has to be a very marked reduction in the lumen as compared with the remainder of the aorta to appreciably reduce the flow.

SUMMARY

The successful relief of cardiac failure in a 16-month-old infant by repair of a coarctation of the aorta is reported.

2. Bahn, R. C.; Edwards, J. E., and DuShane, J. W.: Coarctation of the Aorta as a Cause of Death in Early Infancy, Pediatrics **8**:192, 1951.

3. Sealy, W. C.: Arterial Hypertension Produced by Experimental Stenosis of the Thoracic Aorta, Proc. Soc. Exper. Biol. & Med. **71**:174, 1949.

ENDOMETRIAL CARCINOMA METASTATIC TO THE ISCHIAL TUBEROSITY

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OSSEOUS metastases from carcinoma of the body of the uterus, in contradistinction to those which arise from carcinoma of the cervix, are extremely unusual. Geschickter and Copeland [1] note that "among 86 cases of carcinoma of the uterus or cervix, 5 (5.6%) showed metastases to bone, two of these patients having the primary lesion in the cervix." Williams,[2] in a series of 79 postmortem examinations, found metastases in 16 cases. Although he does not differentiate between fundal and cervical carcinoma, he mentions involvement of the tibiae and innominate bones among the more frequently observed metastatic deposits in the skin, pleurae, peritoneum, lungs, heart, liver, and kidney.

Where studies in corpus carcinoma alone are concerned, the incidence appears to be minimal. Hurdon [3] notes that "metastases are frequent in the lungs and deposits have been found in the tibiae, vertebrae, head of the femur and other bones." On the other hand, she notes that "Warren in 34 autopsies on cancer of the corpus found metastases in the lungs in 18 cases but none in the bones." Cullen,[4] in his classic text, "Cancer of the Uterus," makes no reference to metastatic involvement of the bones from fundal carcinoma. Novak [5] similarly makes no mention of osseous metastases from corpus cancer.

In a series of 266 cases of corpus carcinoma reviewed by Finn,[6] 49 patients showed evidence of metastatic disease, and of these, only 6 (2.2%) presented bony foci. Of 2,067 cases of cancer seen at the Lahey Clinic between 1936 and 1940, Toumey [7] found 95 cases of metastatic cancer to the spine. Of these, only two such cases developed in the fundus of the uterus. (In one of these two patients an osteo-

1. Geschickter, C. F., and Copeland, M. M.: Tumors of Bone, Revised Edition, New York, American Journal of Cancer, 1936.

2. Williams, R.: On the Morphology of Uterine Cancer, Brit. Gynec. J. **11**:529, 1896.

3. Hurdon, E.: Cancer of the Uterus, New York, Oxford University Press, 1942.

4. Cullen, T. S.: Cancer of the Uterus: Its Pathology, Symptomatology, Diagnosis, and Treatment, New York, D. Appleton-Century Company, Inc., 1900.

5. Novak, E.: Gynecologic and Obstetric Pathology, with Clinical and Endocrine Relations, Ed. 3, Philadelphia, W. B. Saunders Company, 1952.

6. Finn, W. F.: Time, Site and Treatment of Recurrences of Endometrial Carcinoma, Am. J. Obst. & Gynec. **60**:773, 1950.

7. Toumey, J. W.: Metastatic Malignancy of the Spine, J. Bone & Joint Surg. **25**:292, 1943.

blastic metastasis developed 19 years after hysterectomy.) Speert [8] found only a single instance (1.8%) of osseous involvement in the 54 cases of corpus cancer reviewed by him. DeCoursey [9] states that although the Armed Forces Institute of Pathology "receives about 40 cases annually of carcinoma of the body of the uterus . . . bony metastases are extremely rare and none have been seen in the AFIP in recent years."

In the combined statistics of all of these reports, the ilium was affected in three cases, the "femur and pelvis" in one case, the vertebrae in six cases, a rib in one case, and the cuboid and metatarsals in one case. In none of these nor in the available literature on corpus carcinoma has any reference been found to true metastatic involvement of the ischium.

In this connection, therefore, the report of the following case, apparently the first of its kind, is thought justifiable.

REPORT OF A CASE

F. G., a 57-year-old white married nulliparous woman, was first seen in September, 1951, complaining of pain in the right hip region of about 10 months' duration. She noted that the pain radiated down the back of the right leg to the big toe and was apparently made worse on sitting. She had been treated by various means, with a diagnosis of "sciatica" due to a low back disability. The patient denied any low back injury, impairment of function in the hip, sensory or motor disturbances in the extremities, or symptoms referable to any other organ or organ system. She noted that the pain had gradually increased despite the use of narcotics so that just prior to her visit she had difficulty not only in sitting but also when lying down. Personal, past, and family history were all essentially noncontributory. A system review failed to reveal any antecedent symptomatology.

Physical examination disclosed a definite flattening of the lumbar spine which did not appear to be related to a localized process in the lumbar spine. The pelvis was level. There was no spasm of the erector spinae group of muscles, no tenderness on percussion over the lower spine, and no evidence of any limitation of motion. The right buttock, however, was somewhat larger than the left, and palpation of this area elicited the sensation of a mass in the gluteal region. On rectal examination a definite bulging of the inner wall of the ischium was disclosed, which was tender and which gave way under pressure with an "egg shell crackle." The hip, knee, and ankle on this side moved freely. There was no impairment of reflex response or sensory perception to light touch, vibration, or pin prick. The motor power was good. Pelvic examination revealed no evidence of any mass, enlargement, or tenderness. The breasts and thyroid appeared benign, and there was no evidence of any regional adenopathy.

Roentgenographic examination at this time revealed a large, expansile, trabeculated bony mass involving the body and ascending ramus of the right ischium (Fig. 1). The lesion appeared to be localized, and, although there were some areas in which the cortex appeared to have been disrupted, the impression was that of a benign tumor. A tentative diagnosis of so-called giant-cell tumor was made. The patient was advised to enter the hospital.

Upon admission to the Hospital for Joint Diseases she was again carefully examined with regard to a primary site of a possibly malignant neoplasm. Physical examination yielded entirely negative results save for the local mass. Owing to mechanical interference and resultant sciatic radiation of pain, operative excision was advised.

On Sept. 9, the right ischium was exposed by the method previously described by one of us (H. M.).[10] Immediately after incision of the skin a large, friable, hemorrhagic mass infiltrating

8. Speert, H.: Endometrial Cancer and Hepatic Cirrhosis, Cancer **2**:597, 1949.

9. DeCoursey, E.: Personal communication to the authors.

10. Milch, H.: Partial Resection of the Ischium: The Operative Procedure, J. Bone & Joint Surg. **17**:166, 1935.

to a slight extent the muscles attached to the ischium was encountered. The tumor mass was excised en bloc from the level of the acetabular protrusion to the symphysis pubis. The wound was closed in layers. The patient made an uneventful recovery, was completely relieved of pain, and was discharged from the hospital on Oct. 3, 1951.

The gross appearance of the tumor was clearly that of a malignant neoplasm. It was described as being "tumor tissue and osseous tissue measuring 8 by 8 by 5 cm. The osseous tissue shows marked destruction. The entire lesion is expanded. On its outer surface there are bits of adipose tissue and muscle tissue. The tumor tissue is markedly friable and somewhat

Fig. 1.—Roentgenogram showing a large, trabeculated, expansile mass involving the body and ascending ramus of the right ischium.

spongy and shows numerous areas of yellowish flecks and linear striations and also shows marked evidence of hemorrhage and degeneration."

The first impression of the pathologist was that this represented a solitary myeloma. Frozen sections, however, disclosed it to be an adenocarcinoma. Subsequent paraffin sections were reported as showing a "metastatic carcinoma to bone. The primary site is one that cannot be determined definitively from the tissue sections" (Fig. 2).

Repeated clinical and roentgenographic examinations in October, 1951, revealed no abnormalities save for the presence of gallstones and the surgical defect in the right ischium. The gastrointestinal series, barium enema, and chest x-rays were all repeatedly negative.

Fig. 2.—Photomicrograph of metastatic lesion in the ischium.

Fig. 3.—Photomicrograph of primary site (corpus carcinoma).

The patient was given deep roentgen therapy to the operative site, portal size 20 by 20 cm., 150 r at a time for a total skin dose of 3,000 r. Roentgenographic reexamination of the region of the right ischium and chest in January, 1952, revealed no evidence of any pulmonary metastasis or metastasis to the ribs above the diaphragm. X-rays of the pelvis disclosed that the bony surfaces of the right ischium were well healed and that there was no evidence of neoplasm in the pelvis or in the adjacent bones.

The patient was well and free of any complaints until April 14, when she first experienced postmenopausal vaginal staining. Pelvic examination at this time revealed the uterus to be irregular and enlarged, and a diagnostic dilatation and curettage were advised. This disclosed a corpus carcinoma. On May 10, 8 months after resection of the ischium and approximately 18 months after the first complaint of sciatic pain, abdominal section was performed by Dr. Paul Topkins at the Caledonian Hospital. The uterus was found enlarged to the size of an eight-week gestation. There was no transmural extension of the tumor, and the adnexae were free of tumor and apparently normal. There was no enlargement of the lymphatic glands and no gross evidence of intra-abdominal metastasis. A total hysterectomy, including both oviducts and ovaries, was performed.

Histological examination by Dr. E. R. Marino revealed no evidence of any malignant growth in the tubes, ovary, or cervix. Sections disclosed "the presence of a malignant invasive neoplasm of endometrial origin. The tumor is proliferating in small and large irregular glandular structures lined by cuboidal and polyhedral cells with large hyperchromatic nuclei. Some papillary production is noted in occasional areas. The underlying myometrium shows invasion of neoplastic tissue, similar to that described. Areas of necrosis are present. The diagnosis is adenocarcinoma of the uterus" (Fig. 3).

When the patient was examined in June, the abdominal and vaginal wounds were well healed, and the general condition was quite satisfactory. In August, she noted slight pain in the leg, but there was no evidence of recurrence either in the soft tissue or in the bony structures. Since that time, she has been able to carry on her normal activities without any hindrance. When last seen in November, 1952, almost two years after the onset of her sciatic complaints, she was well and apparently free of both pain and metastasis.

COMMENT

Although the report of a single case would not seem to warrant any extended discussion, there are certain aspects of this case which should not be passed by with a simple presentation of the facts.

It is to be noted that "sciatica" due to what ultimately proved to be a metastatic lesion was the first and, in fact, only symptom of disease for nearly one year. Presumably the sciatic syndrome resulted from mechanical tension or compression of the sciatic nerve as it passed through the narrow space between the ischial tuberosity and the greater trochanter of the femur. The normally narrow space was evidently further decreased in extent by the presence of a large mass replacing the ischial tuberosity. A similar mechanism must be predicated for the cases reported by Paulson [11] and Nogier.[12]

Although rare, solitary metastases from cancers of the female generative tract are not unknown. Hurdon [8] cites a case seen by Delanoy in which a routine roent-

11. Paulson, E. C.: Neoplasms of Bony Pelvis Producing the Sciatica Syndrome, Minnesota Med. **34**:1069, 1951.

12. Nogier, T.: Osteogenic Sarcoma of the Ischium Diagnosed and Treated as Sciatica, Bull. et mem. Soc. electro-radiol. méd. France **24**:381, 1936; New Case of Osteogenic Sarcoma of the Ischium Treated as Sciatica and Diagnosed by X-Ray, ibid. **26**:112, 1938.

genogram, taken because of pain in the back, revealed a metastatic growth in the upper dorsal vertebrae as the primary manifestation of a corpus carcinoma. Toumey [7] reported two cases of solitary metastasis in the lumbar vertebrae.

Though Warren, Harris, and Graves [13] have suggested that certain osseous metastases, especially those from prostatic cancers, may be accounted for by spread along the perineural pelvic lymphatics, it does not appear that such a mechanism is involved in spread from the uterus. Indeed, a close examination of the data regarding spread of prostatic cancer tends to raise doubt as to the actual clinical importance of spread via the perineural lymphatics, even in this condition. The pattern of spread from the uterus appears far more likely to be that of the vertebral venous drainage of the area. The vertebral venous system, first and so well described by Breschet,[14] has recently been reevaluated by Batson,[15] and, although no details are given specifically relating to the ischial drainage, it appears that this system of vessels quite satisfactorily explains the peculiar distribution of osseous metastases seen in fundal carcinoma.

Prognosis, however, depends less on the presence of metastatic foci than it does on the local anatomical extent and histologic degree of differentiation of the primary neoplasm. As a general rule, endometrial carcinoma is noted for the tendency to metastasize relatively late in its biological course. Often several months to a few years may elapse before metastatic foci are discernible. On the other hand, once a metastasis has appeared, prognosis is not necessarily imminently grave.

The patient reported on here is alive and completely free of symptoms or demonstrable metastases nearly two years after the onset of her initial complaints. One of Toumey's [7] patients was apparently well for 19 years following hysterectomy until the appearance of a spinal metastasis. In one case reported by Finn,[6] in which metastasis to the cuboid and metatarsals occurred two months following hysterectomy, the patient was alive and apparently free of metastasis six and one-half years after midcalf amputation.

In this connection, Finn noted that 18 (62%) of 29 patients with extrapelvic (Stage 5) fundal carcinoma had recurrence of their neoplasm and survived only six months after removal of the primary tumor. On the other hand, six of seven patients with solitary and localized extrapelvic metastases were alive and apparently free of tumor one and one-half years after the removal of both the primary and metastatic foci.

He further notes that "no recurrences have been cured by x-ray or radium irradiation. Extensive pelvic surgery for solitary and localized recurrences has shown encouraging results, even though the number of patients so treated is very small." Although no statement can be ventured as to the ultimate outcome in the present case, the progress made thus far has amply justified the patient's treatment. It may not be too bold to suggest that solitary osseous metastasis without other involvement should be surgically removed if at all technically possible.

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13. Warren, S.; Harris, P. N., and Graves, R. C.: Osseous Metastasis of Carcinoma of the Prostate, with Special Reference to the Perineural Lymphatics, Arch. Path. **22**:139, 1936.

14. Breschet, G., quoted by Batson.[15]

15. Batson, O. V.: The Function of the Vertebral Veins and Their Role in the Spread of Metastases, Ann. Surg. **112**:138, 1940; The Role of the Vertebral Veins in Metastatic Processes, Ann. Int. Med. **16**:38, 1942.

SUMMARY

A case of tumor of the ischium is presented in which sciatic radiation of pain was the patient's only complaint. Resection of the ischium for purely mechanical purposes led to prompt subsidence of symptoms. The tumor proved to be a metastatic carcinoma, the nature of which was not disclosed until eight months later when hysterectomy was performed for postmenopausal vaginal staining. This appears to be the only case in the available medical literature in which a corpus cancer metastasized solely to the ischial tuberosity. It is suggested that metastasis occurred via the tributaries of the vertebral venous system or, less likely, by perineural lymphatics. The patient is well, symptom-free, and roentgenographically apparently metastasis-free nearly two years after her initial complaints. It is further suggested that solitary osseous metastases without other evident involvement be surgically removed if at all technically feasible.

Dr. Paul Topkins and Dr. E. R. Marino, of the Caledonian Hospital, and Dr. Henry Jaffe, of the Hospital for Joint Diseases, gave permission to use material reviewed by them.

UNUSUAL PROTRUSION OF PREPERITONEAL FAT IN SUBCUTANEOUS TISSUE

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THIS CASE is being reported because of the unusual type of congenital defect that existed in the insertion of the rectus abdominis muscle and the pathology that developed secondarily to it which necessitated surgical correction.

ANATOMICAL CONSIDERATION

The normal insertion of the rectus abdominis muscle [1] is by three portions of unequal size into the cartilages of the fifth, sixth, and seventh ribs. The upper portion, attached principally to the cartilage of the fifth rib, usually has some fibers of insertion into the anterior extremity of the rib itself. Some fibers are occasionally connected with the costoxiphoid ligaments and the side of the xiphoid process. The rectus sheath is formed normally by the aponeurosis of the obliquus externus, obliquus internus, and the transversus muscles. At the lateral border of the rectus muscle they form two membranes, the anterior and posterior lamellae of the sheath. The aponeurosis of the internus, above the umbilicus, splits into two lamellae, one of which passes anterior to the rectus muscle and fuses with the externus; the other passes posterior to the rectus muscle and fuses with the aponeurosis of the transversus muscle to form the posterior lamella of the sheath. Above the costal margin, to which the internus is attached, the costal cartilages and xiphoid process of the sternum take the place of the aponeurotic sheath, posteriorly. The posterior lamella of the internus aponeurosis is attached normally to the cartilages; the anterior lamella ends abruptly in a fibrous band similar to the linea semicircularis, the rectus muscle above this point being covered only by the externus aponeurosis. In the case that is being reported, the rectus abdominis muscle inserted into the cartilage of the seventh rib only and failed to reach the cartilage of the fifth or the sixth rib.

REPORT OF A CASE

Private D. F. T. was first seen at the surgical clinic of the United States Air Force Hospital, APO 919, on Sept. 10, 1952, after being referred there from morning sick call. His chief complaint was that every time he performed any duty requiring exertion, anterior chest pain developed, with the appearance of a small mass at the infrasternal border. He stated that as soon as he ceased straining the pain subsided, and by utilizing the slightest amount of external pressure he was able to reduce the mass. History revealed that the first occurrence was six months previously while he was helping to build a parking lot at Fort Bliss, Texas. He lifted a cement block and substernal pain developed. It was then that he first noticed the infrasternal mass. Whenever he has strained since then, he has noticed the infrasternal midline bulge with the associated pain. The pain radiated laterally in each direction, and he stated, "crossed under my

1. Lewis, W. H.: Anatomy of the Human Body, Ed. 23, Philadelphia, Lea & Febiger, 1936, p. 408.

ribs." He was always able to reduce the size of the bulge by simply exerting pressure on it. A routine history revealed that he worked in the office of an electrical wholesale corporation prior to his entry into service and that he entered service in January, 1952. He smokes a pack of cigarettes a day, and he drinks an occasional glass of beer. The family history was noncontributory, and the patient had had the usual childhood diseases, with no complications or sequelae. He denied any previous hospitalization.

He was admitted to the surgical service on Sept. 12, and received a routine preoperative work-up. The blood count, urinalysis, chest x-rays and blood serology revealed nothing abnormal. The electrocardiogram was interpreted as being normal. Physical examination revealed a well-developed, well-nourished, 22-year-old man in no acute distress. The entire examination was essentially noncontributory; however, when he was asked to strain and increase his intra-abdominal pressure, as on lifting a heavy object, a small walnut-sized mass appeared at the infrasternal border. This mass was nontender, smoothly outlined, and reducible as soon as the straining ceased. The preoperative diagnosis of an epigastric hernia was established.

The following day the patient was given general anesthesia and was placed in the supine position. A midline incision 2 cm. long was made from the xiphoid process inferiorly. The anterior rectus sheath was found to be intact and was incised longitudinally. The rectus muscle was found to be in complete apposition in the midline but was found to insert only on the costal cartilage of the seventh rib and did not insert on the costal cartilage of the fifth or sixth rib. The rectus muscle was then separated in the midline, and the posterior rectus sheath was examined and noted to be normal. At this point while the patient was under anesthesia a hiccough reflex started to develop as the anesthetist was adjusting his endotracheal tube. It was noted that a small pad of fat lying in the defect between the insertion of the rectus muscle and the xiphoid process moved up and down. Under close examination it was found that this adipose tissue was freely movable and extended posterior to both the rectus muscle and the posterior rectus sheath inferiorly. A probe was then extended inferiorly behind the posterior rectus sheath alongside the fat pad. The posterior rectus sheath was then incised, and it was noted that the probe was located between the peritoneum and the posterior rectus sheath and that the fat pad originally noted was connected to and part of the preperitoneal fat. Actually, therefore, the pathology consisted of preperitoneal fat herniating through a congenital defect in the insertion of the rectus abdominis muscle into the subcutaneous tissue. The adipose tissue was then replaced into its normal anatomical position. The defect through which the fat originally passed was then closed by first suturing the posterior rectus sheath up to the level of the fifth costal cartilage and by doing the same with the anterior rectus sheath. This repair obliterated the defect which was previously present between the level of the seventh costal cartilage and that of the fifth costal cartilage and therefore prevented any further protrusion of preperitoneal fat into the subcutaneous tissue.

The patient had an uneventful postoperative recovery and was discharged from the hospital to duty six days after the surgical procedure. Though follow-up was limited in duration, no recurrence of symptomatology was revealed.

COMMENT

This case has been presented because of the unusual type of congenital defect which was found. This defect consisted in the short abnormal insertion of the rectus abdominis muscle only on the seventh costal cartilage and failing to reach the costal cartilage of the fifth or sixth rib. The preperitoneal fat was therefore able to protrude through this defect into the subcutaneous tissue on exertion with an increase in intra-abdominal pressure. This resulted in sufficient pain to prevent the patient from performing any strenuous work. It is also to be noted that if the hiccough reflex had not developed while the patient was under anesthesia the pathology might not have been detected.

SUMMARY

A congenital defect existing in the insertion of the rectus abdominis muscle is reported.

PARATHYROID ADENOMA WITH NEUROLOGIC SYMPTOMS

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DURING the past 25 years, primary hyperparathyroidism due to hypersecretion by one or more true adenomas of the parathyroid glands has become a well-founded disease entity. From the literature it is evident that up to the present there have been well over 500 such cases reported. In addition, there have recently been very excellent and complete reviews of the literature on parathyroid adenoma.[1]

The following is a case report of a parathyroid adenoma discovered early in the disease process, with primarily neurologic symptoms.

REPORT OF A CASE

R. M., a 31-year-old white man, entered the Baylor University Hospital surgical clinic in September, 1951, with a complexity of complaints of four months' duration. The family and past history were essentially noncontributory. The most predominant symptoms were the sensation that he constantly had a lump in his throat which interfered slightly with swallowing and that he had a sensation in his neck as if his collars were too tight, although they were always unbuttoned. These symptoms had been present over the past four months and had remained about the same. In addition, the patient complained of a tingling, occasionally, numb sensation in the entire left arm, sometimes involving the shoulder, neck, and the entire head, which had occurred four or five times in the past five years. These attacks would last approximately 15 minutes at a minimum to two hours at the maximum. With these changes in his upper extremity, he had an associated photophobia and blurring of vision, and, on a few such occasions, his wife told him that his "eyes appeared dilated." These attacks of visual disturbances were apparently not at all related to activity, time of day, or any other environmental or habitual factor.

Over the past few years, also, postprandial eructation developed, with a sour taste in the mouth, and vague indigestion consisting of a mild epigastric burning pain, usually after eating very rich or greasy foods. He had lost approximately 8 lb. (3.6 kg.) over the past six months and had increased fatigability over the past few years.

The patient gave a history of having passed two kidney stones, one in 1949, for which he was hospitalized, and one approximately 12 months ago. Each episode lasted approximately 12 hours, with a severe crampy suprapubic pain radiating to both testicles, with some burning on urination. His local physician told him that he had blood in his urine during these attacks, although this was not obvious to the patient grossly.

Physical Examination.—The physical examination was insignificant, except that the patient had a moderate myopia for which he wore corrective glasses. Inspection, palpation, and auscultation of the neck, specifically were noncontributory.

From the Department of Surgery, Baylor University Hospital.

1. Norris, E. H.: Internat. Abstr. Surg. in Surg., Gynec. & Obst. **84**:1-41, 1947. Mandl, F.: Surgery **21**:394-440, 1947. Black, B. M.: Surg., Gynec. & Obst. **89**:172-182, 1948.

Results of routine laboratory studies were within normal limits. Blood serum calcium and phosphorus determinations were suggestive of hyperparathyroidism. These values were rechecked shortly and then followed over the subsequent several weeks, revealing blood serum calcium levels ranging between 12.4 and 14.0 mg. per 100 cc. and blood serum phosphorus levels ranging between 2.1 and 3.0 mg. per 100 cc. X-ray examination of the chest revealed nothing abnormal. Dental x-rays revealed intact lamina dura. The patient was admitted to Baylor University Hospital on Dec. 2, 1951.

A barium swallow revealed no evidence whatever of diverticuli, filling defect, stricture, varices, or other esophageal abnormalities. An intravenous pyelogram revealed normal renal function bilaterally, with no evidence of obstruction, ectasia, or other abnormalities. There was, however, a small single calcification a few millimeters in diameter in the lower pole of the left kidney, well into the parenchymal tissue. Numerous skeletal films revealed no evidence of abnormal calcification or demineralization, either generalized or localized. As an inpatient, the blood serum calcium and phosphorus levels persisted in the previously noted abnormal pattern, the calcium levels remaining above normal and the phosphorus levels remaining low. A few scattered phosphatase determinations were within normal limits. The determinations for serum proteins were within normal limits.

All joints were hypermobile with lax muscles; the patient easily placed either foot behind his head without undue strain. The neurological examination was completely negative. During the eight days that he was in the hospital prior to surgery, he was given a low calcium diet, but the Sulkowich test for calcium in the urine consistently resulted in 4+ or heavy cloud determinations, and the serum calcium remained at the same high level. The evidence at hand therefore was highly suggestive of early hyperparathyroidism.

Operation.—On Dec. 10, 1951, with the patient under general endotracheal anesthesia, exploration was carried out through a classic Kocher collar incision. Dissection was first started in the region of the inferior pole on the right side. The inferior thyroid artery and the right recurrent laryngeal nerve were identified, followed by very careful gentle dissection lateral to the trachea, between the trachea and esophagus, between the esophagus and the prevertebral fascia and the longus colli muscles, and in the right posterior superior mediastinum. The right inferior parathyroid gland was fairly easily identified and found to be slightly smaller than normal and to have a typical vascular pedicle. Dissection was then carried to the upper pole of the right lobe of the thyroid; no parathyroid tissue whatever could be identified, despite a very tedious search. Dissection was then carried out in this area along the hypopharynx and the carotid sheath and between the esophagus and prevertebral fascia just anterior to the longus colli muscles, again without disclosure of an adenoma. The right posterior superior mediastinum was again explored both by direct vision and by gentle blunt palpation, with negative results. The isthmus of the thyroid gland was then elevated from the trachea anteriorly and superiorly, and this area was carefully explored, with no abnormal finding. Then dissection was commenced at the inferior thyroid pole on the left side of the neck, and no parathyroid tissue whatever could be found in this area. Dissection was next carried out in the left posterior superior mediastinum by direct vision and palpation, this also proving fruitless. Dissection was then carried superiorly, and, as the upper pole of the thyroid gland was mobilized, a small but definite tumor mass was noted. It lay along the anastomotic arch between the inferior and superior thyroid arteries behind the midupper portion of the left thyroid lobe and had a vascular pedicle which arose from one of the inferior ramifications of the superior thyroid artery. The tumor appeared to have a thin transparent capsule and was moderately firm in consistency. The pedicle was ligated, divided, and the tumor easily removed in its entirety. A frozen section of the tumor was reported as an adenoma, type undetermined, compatible with parathyroid adenoma. The wound was closed in layers in routine fashion with interrupted sutures of black cotton. The patient had withstood the procedure well.

Pathological Examination.—The specimen was described as a well-circumscribed nodule of soft tissue of chestnut-brown color, apparently encapsulated by a glistening, intact, transparent membrane, weighing 0.48 gm. and measuring 1.2 by 0.9 by 0.3 cm. Microscopic examination revealed an encapsulated glandular tissue which consisted of closely aligned oxyphilous cells, occasionally arranged into small groups and cords, with the principal cells being loosely arranged

in wide sheaths. Interstitial fat tissue was absent, and there was an irregular distribution of fine bands of fibrous tissue. There was a distortion of the normal architecture, as previously described, with a moderate variation in the cell size and structure.

Diagnosis.—The final pathological diagnosis was parathyroid adenoma of the mixed type.

Postoperative Course.—The patient had a completely uneventful convalescence, with the exception of a faintly positive Chvostek sign present from the second to the fourth postoperative day. Twenty-four hours after operation, the blood serum calcium had dropped to 11.8 mg. per 100 cc., the lowest it had been. Forty-eight hours later, it was within normal limits for the first time at 10.9 mg. per 100 cc. and remained normal subsequently. Sutures were removed on the second and third postoperative days, and the patient was discharged on the fifth postoperative day to be followed in the outpatient clinic.

For the first four to five weeks postoperatively, the complaint of occasional numbness in the back of his head and in the arm, with some generalized weakness, persisted. However, over the subsequent three months, the patient resumed his previous occupation of working in a road gang and has been able to perform his duties without any difficulty, his strength returning to normal.

On reexamination nine months later, the patient was found to be completely free of the preoperative neurological symptoms, except for a vague sensation of fullness in his neck, which he localized to the region of the incision. Physical examination disclosed no abnormality in the neck except for the well-healed incision. Serum calcium and phosphorus determinations done at this time remained normal.

COMMENT

A case of a solitary parathyroid adenoma associated with hypercalcemia in a 31-year-old white man is reported, in which the presenting complaints were chiefly neurologic, all of which had disappeared completely 10 months after removal of the adenoma, with the exception of a vague sense of fullness in the region of the incision. The adenoma weighed only 0.48 gm. Blood calcium levels returned to and remained normal after operation.

Clinical Notes, New Instruments and Techniques

MODIFIED T-TUBE USEFUL FOR INTUBATION OF NONDILATED COMMON DUCTS

GEORGE E. MOORE, M.D.
MINNEAPOLIS

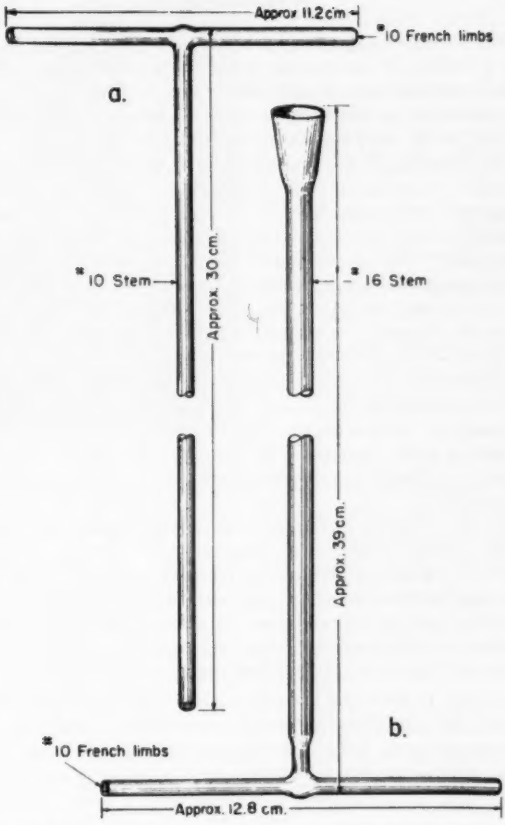
THE NUMEROUS T-tube designs reported in the literature and available commercially are ample evidence that no single one is adequate for the manifold variations of common duct pathology encountered during surgery. Several annoying experiences with the intubation of common ducts which would admit a T-tube no larger than a No. 8 or 10F indicated a need for a redesigned T-tube for these particular cases. If one wishes to drain such a duct there are three immediate alternatives: (1) use of a standard No. 8F T-tube, (2) use of a small straight cathether of rubber or polyethylene, and (3) use of a fabricated catheter, such as a ureteral catheter. The advantages of using a standard small-sized T-tube are negated by the flexibility and ready collapsibility of the long thin-walled stem and the difficulty in securing it to a glass or metal adapter with an adequate lumen. An additional expedient, suggested by R. L. Varco, is to slide a large catheter over the stem so as to protect it.

On the opposite page is a drawing of a standard T-tube (*a*) and a T-tube (*b*) designed to overcome some of the handicaps mentioned (Figure).

This T-tube has the following advantages: (1) small-sized limbs and neck for use in tiny ducts in which the exploratory opening should be kept as small as possible, (2) sturdy-walled stem of a larger caliber, and (3) a tapered adapter-end for convenient connection to glass or metal adapters.

Such a tube has been fabricated by C. R. Bard, Inc., Summit, N. J.

Present address: Roswell Park Memorial Institute, Buffalo, N. Y. (Dr. Moore).



Drawing of a standard T-tube (*a*) and a T-tube (*b*) designed to overcome handicaps described in text.

SIMPLIFIED DRESSING FOR BURNED HANDS

NORMAN F. RICHARD, M.D.
SHELBYVILLE, IND.

Because of the possibility that some may not be familiar with this method, I consider it worth while to describe a simple yet effective way to deal with burned hands. My colleagues and I have employed this treatment in a considerable number of cases and have been impressed by the good results obtained. It is applicable to nearly all burned hands, regardless of the degree of the burn, inasmuch as the same surgical principles are involved in each instance.

Since all thermal burns should be sterile by the very nature of the injury, they should remain so until contaminated by droplet infection (commonest [1]) or by contact with clothing, hands, nonsterile dressings, etc. No attempt is made to "clean up" the injured part unless it has been covered with butter or otherwise grossly contaminated. In this event, under general anesthesia, the hand is soaked in an isotonic sodium chloride solution containing a detergent such as "Joy." Needless to say, all attending personnel are masked, and strict asepsis is observed. Loose fragments of skin are trimmed off with scissors, but no attempt is made otherwise to débride the wound, since the depth of a burn is not always evident at this early stage. Soft cotton balls are an aid in removing the greasy covering if present.

The dressing itself consists of a sterile white cotton pallbearer's glove [2] which has been prepared previously with petrolatum and kept in a sterile container. The glove is easily slipped on the hand, being careful to avoid wrinkles or folds. Next, sterile sheet wadding is applied in sufficient amount and in such a way that firm even pressure will be applied to all surfaces by the elastic bandage which forms the outermost layer. The resulting bandaged hand somewhat resembles a boxing glove.

A record is kept of the patient's temperature during the ensuing days, and if signs of infection appear a broad spectrum antibiotic is administered. Very little sedation is required after the first 24 to 48 hours. Rarely is the dressing removed for inspection before the seventh day. At the end of this time the glove is cut off with sterile scissors. If the burn has been of first or second degree, healing will be well advanced. If a third-degree burn has been incurred, an estimate can be made of the amount of skin grafting required. Usually two weeks are required for the establishment of a bed of granulation sufficient to support a graft.

The gloves are made in three sizes: small, medium, and large, and each will fit either the right or the left hand. As many gloves as desired are placed flat in a glass or metal container and covered with melted petrolatum. They are then autoclaved for 20 minutes at 15 lb. (6.8 kg.) pressure and a temperature of 250 F. The resultant dressing is sterile and inexpensive. It possesses a fine mesh and is easy to apply, conforming closely to the part being bandaged.

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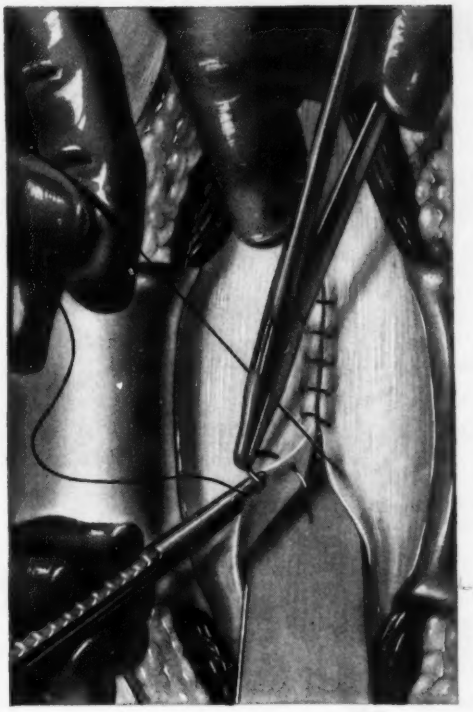
From the Inlow Clinic.

1. Meleney, F. L., and Stevens, F. A.: Postoperative Haemolytic Streptococcus Wound Infections and Their Relation to Haemolytic Streptococcus Carriers Among Operating Personnel, Surg., Gynec. & Obst. **43**:338-342 (Sept.) 1926.

2. Obtainable from Monte Glove Co., Shelbyville, Ind.



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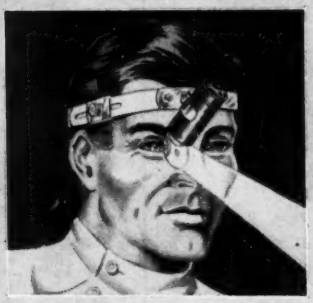

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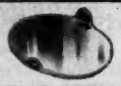

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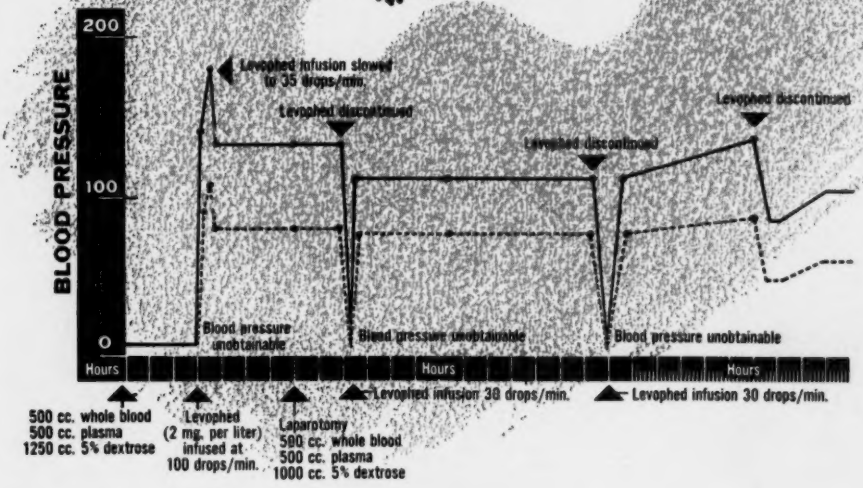

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